

One Swallow—Will There be a Summer?

At first sight it seems as if the new communications satellite launched by Intelsat at the weekend will have been a success. After the technical disappointments of the past few years, the architects of Intelsat need something to cheer them up. So far, the communications satellites in synchronous orbit have been comparatively crude affairs. Although the band width of the Intelsat III instruments (500 MHz) is great enough to accommodate more than 1,000 telephone circuits, and in spite of a certain amount of directionality provided by the spin stabilization of the satellite, for practical purposes the Intelsat III satellites have been spreading their signals over a much greater area on the surface of the Earth than has been strictly necessary, with the result that power consumption has been extravagant. To be sure, there is no more reason to complain about the inadequacies of the design of the Intelsat III series of satellites than there would have been, in the mid-twenties, to have complained that the Model T Ford was inferior to some other designs then coming on to the market. The fact remains, however, that the Intelsat IV satellites, four of which are eventually to be launched, will be able to point antennae at transmitting or receiving stations on the ground in such a way that more economical use is made of electrical power and less interference is caused with other potential occupants of the synchronous orbit above the Equator. If the Atlas-Centaur rockets intended as launchers for Intelsat IV manage somehow to perform more successfully than the launchers for Intelsat III—two out of eight of them failed—and if the satellites themselves function properly, Intelsat IV should be not merely a marked improvement on the present system of satellite communications but also a more economical method of long distance telecommunication—the satellites are built to last seven years and will be able to handle up to a dozen television cameras at once.

If the seventy-seven member nations of Intelsat are made cheerful by last weekend's news, however, they should reflect that technical progress can win only half the battle which lies ahead of them. For the best part of two years, Intelsat has been wrestling with the problem of how to set up permanent arrangements for the international telecommunications system which it exists to operate. Although the next meeting of the Preparatory Committee in April and May this year may finally agree on a constitution for the next few decades, there is still a chance that the negotiations will founder on the question of who gets what contracts—a familiar part of negotiations within European organizations such as ESRO and ELDO. In any case, the constitution likely to emerge from this tedious negotiation is far from satisfactory. For one thing, it seems now to be accepted that the American organization Comsat will remain the manager of Intelsat for a period of six years after the agreement has been signed. Second, it now seems probable that there can be no substantial broadening of the geographical scope of Intelsat and that, in particular, the arrangements being made by the Soviet Union under the banner of Intersputnik will be separate

from those of Intelsat. Finally, there is a serious danger that the policy makers of Intelsat will so faithfully embody the more conservative elements of the national telecommunications agencies in the 77 member nations as to cast a pall of dullness over all Intelsat's works.

The issue of Comsat as manager is a serious offence against good management. Comsat itself is a strange creation, half publicly owned and half privately owned (with the chief United States telecommunications companies in strong positions). Originally President Kennedy's intention seems to have been to allow private capital a chance to participate in a new development without entirely laying his government open to the charge that private industry was being allowed to make new vast fortunes out of publicly supported research and development on rockets and satellites. In the event, however, Comsat has become an important instrument of American international policy—formally it represents the United States in Intelsat, for example—as well as a telecommunications company in its own right which is now planning to collaborate with the American Telephone and Telegraph Company in the launching of a telecommunications satellite for domestic use within the United States. (Those in Britain who are at present toying with proposals for nationalization by halves should regard the example of Comsat as a warning that there are often serious limitations on what can sensibly be done.) Since the beginning of Intelsat, Comsat has been charged with responsibility for day to day management of the satellite system for which the international consortium has paid, but from the beginning there has been trouble about the precise meaning of this role. Some member governments have at various times been hoping for a manager resembling an executive agency which carries out the policy laid down by the international committee, but Comsat's interpretation of its task has seemed more often to assume that to be manager is to be endowed with almost all the power that matters. The fact that it has now been agreed that this period of delegated responsibility will come to an end six years after a final agreement is signed is at least one step in the direction towards equitable management of Intelsat's affairs, but it is only prudent to acknowledge that six years from now the whole pattern of international telecommunications will have been determined once and for all. In retrospect, it may then seem only fair that the pattern should be predominantly American—none of Intelsat's satellites would have functioned without American rockets and development. But the headstrong way in which Comsat functions will also seem a bitter pill to have swallowed.

This is why it is a pity that the issue of management has been clouded by the view (most strongly advocated by European members of Intelsat) that there should be a wider distribution of contracts for the building of the satellite system. The difficulty here, of course, is that if the comparatively advanced nations of Western Europe benefit from subcontracts with American primary contractors not merely in money but in expertise, this may



increase the cost of the system as a whole to those members of Intelsat not yet in a position to win contracts or subcontracts. The problem is well illustrated by the construction of the eight Intelsat IV satellites (four spares) now waiting to be launched. After pressure from would-be subcontractors, just over 26 per cent of the \$54.8 million paid by Comsat to the Hughes Aircraft Company was laid off in subcontracts with companies in Western Europe, Sweden, Canada and Japan. This was in European eyes a great improvement on the pattern of subcontracts for Intelsat II and Intelsat III, when 2 per cent and 6 per cent of the prime contracts respectively were laid off to subcontractors. But in the past year, when Comsat as manager of Intelsat has been required by its international committee to make the cheapest arrangements, not the geographically most equitable arrangements, for building the second set of four satellites, virtually the whole cost (\$20.9 million) has been spent in the United States. The moral to be learned from this is of course that if European companies wish to bring about a rapid increase of their technical skills, they must seek to do this not by hoping for contracts which they cannot hope to win competitively but, rather, by spending money on research and development or by making commercial links with companies in the United States. For European governments, and the British Government in particular,

it is foolish to make a song and dance about the way in which Intelsat contracts are awarded when opportunities for fruitful development of a literally mundane character in telecommunications are consistently neglected.

With the kind of treaty now in prospect, the chances are that the development of Intelsat in the years ahead will be determined by largely commercial considerations and in many ways this is as it should be. There is plenty of painful experience to show the folly of hoping that technological developments can bring political as well as economic benefits, which is why it would be wrong to hope that the mere existence of satellites in synchronous orbit will make it easier for Russians and Americans to talk civilly to each other. At the same time, however, it is reasonable to expect that the existence of communications satellites will help enormously in the development of regions such as Latin America, and to this extent the value of the Intelsat network as a kind of international public service should not be entirely discounted. It is in particular important that in the years ahead, working arrangements with the Russian satellite network (still innocent of even a development satellite in a synchronous orbit) should be carefully worked out. The conference of the International Telecommunications Union later this year should be an opportunity for giving Intelsat this wider perspective.

Pay as You Learn

THE National Union of Students in Britain came out last week with a stirring declaration that there should be an immediate increase of £70 in the annual value of the grants made by local authorities to students from the present basic rate of £380 to something like £450, the kind of increase necessary to restore the value eroded away by inflation in the past decade. By all accounts the union is also seeking to ensure that students following courses leading to higher awards which are not necessarily degrees—a Higher National Diploma, for example—should be dealt with as are the luckier students. The students are also asking for a revision of the system under which, at present, students with parents whose income exceeds £900 a year receive only a proportion of the basic grant. By the standards of some of the pay claims now being made in Britain, all this is modest enough, but the National Union of Students would do well to recognize that its claim for better treatment has entirely overlooked the ways in which there might be organized a radical revision of present arrangements for supporting students at British universities. With finances so much under pressure, has not the time come for another look?

First of all, there will be general agreement with the view of the National Union of Students that the means test is an anachronism. Only a year ago, the government seemed willing to accept the view of the House of Commons that young people become responsible adults at 18. In this sense, it is absurd that the same young adults should be dealt with at the universities in ways that bind them financially to their facilities for the whole duration of a university course. In circumstances as in Britain in which students cannot easily earn for themselves substantial nest eggs in the long vacation and in which the general supposition that university education should be free, casts a spell of inactivity over many students, the means test seems now

to have created a new class of impoverished students—those with families sufficiently well-to-do to be required by the means test to pay up for their sons and daughters but for one reason or another unable or unwilling to do so. Whatever the abolition of the means test might cost the government—one estimate is £12 million a year or something like 15 per cent of the present cost of maintaining students at universities—the time has come when it should be done away with. And university teachers as well as students should band together to resist the notion that there should be an upper limit in age (perhaps 21) for the applicability of the means test so that students would be encouraged to take a year off between school and university.

The National Union of Students is on much less sure ground in its claim for a general increase in the rate of grants. To be sure, there has been a sharp increase in the cost of living and £380 is no longer enough to keep a student for a year in academic life. But is it therefore essential that the increase should be paid for out of public funds without any qualification? One difficulty is that of knowing whether this claim on the resources available for higher education should take precedence over other needs—research, recruitment of teachers to the polytechnics and the provision of more undergraduate places at the universities for example. For the system as a whole, it might be much better if the money were spent elsewhere, which is why the students should examine for themselves some of the other ways in which money might be provided by other routes. To devise ways of making vacation jobs easier to come by, the National Union of Students could itself also do a great deal to encourage the setting up of scholarships to deal with needy cases. And the time has now arrived when serious attention should be given to the arguments for and against the financing of

higher education by means of loans of one kind or another.

The arguments one way and the other have recently been summarized by Maureen Woodhall in a book published for the University of London Institute of Education (*Student Loans*, George G. Harrap & Co. Ltd, 45s). The starting point for this valuable study is the experience of Scandinavian countries in the operation of loan systems. Denmark, Norway, Sweden and Finland have for decades financed a great deal of the cost of higher education in this way. Each of them has its own arguments to make against the view of those who fear that student loans can have only evil consequences. Certainly in Scandinavia there is no reason to think that relatively poor families are discriminated against more severely by the loan system than they are by poverty alone. Miss Woodhall is, however, wise to draw attention to the way in which the widespread acceptance of loan financing in Scandinavia stems in part from the way in which the system predates the great expansion of university numbers in recent years. Nobody could guarantee that a system that works well in Scandinavia would function at all in the very different circumstances in Britain in which, among other things, it is assumed that higher education should be for practical

purposes free. At the same time, it is plainly quite untrue to argue that student loans would place an intolerable burden on young people in the years immediately after graduation—if the extra £70 a year for which the National Union of Students is now asking were made available as a loan and not a grant, it would be entirely possible for most graduate students to make full restitution within three years or so. In any case, it would always be possible to shade the starkness of the system by arranging that repayments would be linked to starting salaries or some other index.

But is this not the thin end of a nasty wedge? That is what the students ask. And of course it would be a great step back if the British university system were to become again a privileged preserve. In practice, however, there is no danger that any government will be able to pretend that the demand for higher education can be ignored—the product of the system is far too important to be dispensed with. And what the students might gain from a recognition that the public purse is not the only source of money is a unified system of grants and loans applicable not merely to those at universities and polytechnics but, equally important but frequently forgotten, the students at colleges of education as well.

No Right to Die ?

THE British Medical Association has never been known for its capacity to move ahead of the times—by all appearances, the association has to struggle to keep up with lay opinion, as its timorous and unwilling acceptance of abortion legislation has shown. Its latest declaration on social policy, a report on euthanasia published this week (*The Problem of Euthanasia*, BMA, 3s), may be right in its chief conclusion that voluntary euthanasia should not be legalized, but it is at once muddled and complacent in its argument. Briefly, the special panel set up for the purpose under Dr H. C. Trowell (who is religiously as well as medically qualified) has concluded that it would be “impossible to provide adequate safeguards” in legislation to permit voluntary euthanasia in the sense that there would certainly be errors of prognosis and errors in the decisions of patients suffering from chronic or terminal disease that the time had come to put an end to life. In general, of course, there is much weight in these arguments and also in the view that doctors brought up instinctively to believe their task to be the preservation of life would be perplexed and possibly demoralized if they were told that they must also occasionally put an end to life. One of the panel’s arguments is that if the “right to die” were legally accepted, doctors would be at a loss to know whether to resuscitate unsuccessful suicides. But the panel also says that death is usually a peaceful process, that some of the chronic diseases most distressing to patients and relatives will ultimately benefit from research and that society should spend more effort on the care of the chronic sick.

The most serious defect of this line of argument is that it quite ignores those parts of the case for legalized euthanasia which deserve to be taken seriously. To begin with, there seems to be a substantial number of the elderly and chronic sick who want not to live. Their reasons may have nothing to do with their physical condition but may instead be born of loneliness or frustration. To say that these people have no pain is beside the point. Second,

at a time when it is proper to expect that all rational questions should be answered, it is a great intellectual difficulty to know how a person’s request to die shall be denied. By dodging this issue, the panel on euthanasia has simply fallen back on the old precept that the patient never knows best. And on the need for better care for the elderly and chronic sick, the panel makes it plain that it is more concerned with the problems of severe pain and disability than with the emotional and psychological discontents of those who want to die.

The unsuccessful attempt in the last Parliament by Dr Hugh Gray to carry his Voluntary Euthanasia Bill should in short have been a powerful stimulus to British doctors as well as their customers to worry constructively about the problems which arise. Most probably the panel is right in saying that the risks of euthanasia legislation would be unacceptable but it is timorous and unimaginative in suggesting how a real problem might be made to go away.

100 Years Ago



The Eclipse Expedition

How about the Eclipse Expedition, which, I presume, you helped to sanction? I informed the public that it would prove a complete swindle, and so it has turned out. As long as such professional liars as the Astronomical Society are allowed to gull the nation, what chance is there of arriving at the truth?

JOHN HAMPDEN

From *Nature*, 3, 267, February 2, 1871.

OLD WORLD

DRUG DEPENDENCE

Lack of Knowledge

A REPORT on drug dependence, published this week by the World Health Organization, is a salutary reminder of the lack of knowledge about drug addiction. Drawn up by an expert committee on drug dependence, the report (WHO Technical Report, No. 460, 1970; 6s) makes a few tentative suggestions and offers one or two conclusions, but the chief message to emerge is that more research—both sociological and pharmacological—needs to be done before any course of action for treatment or prevention of drug addiction can properly be evaluated. But the report does provide a useful, if sketchy, review of the various methods and goals of treatment and prevention, and it offers one clear recommendation—that the drug propiram should be considered as a dependence-producing drug comparable with codeine. The committee therefore suggests that propiram should be brought under the terms of the 1931 convention on narcotic drugs.

Unfortunately, there are almost as many hypotheses about the onset of drug dependence as there are experts to make them. The factors involved are usually closely linked with the psychological make-up and the social environment of the individual drug taker, and it is therefore difficult to make generalizations about the efficacy of various methods for preventing widespread drug dependence. But the WHO committee points out that psychosomatic disorders clearly could not result in drug dependence if access to drugs is denied. The committee therefore believes that legal control of the distribution of drugs is one of the most important means of controlling drug abuse, but suggests that “the most pressing need is to understand the various mechanisms of spread—for example, the parts played by the confirmed users of various types of drug”.

But legal controls on drugs that are over-ambitious are likely to be unrealistic and self-discrediting, the committee warns. In particular, possible harmful effects must be borne in mind, for example “rapid suppression of the use of opium might lead to the introduction of other drugs, such as heroin or drugs of the amphetamine, barbiturate or other types”. In the face of the uncertainty about the efficacy of legal controls, it is reasonable to hope that education may help to deter potential users. But the committee pours cold water on such hopes, at least in the immediate future, suggesting that “there are many reasons to doubt” that simple educational programmes will be sufficient to prevent drug dependence. Nevertheless, the

committee suggests that educational measures should be directed towards changing the attitudes of the community toward drugs in general. “The advertising of pharmaceutical products in some countries may have had the result of encouraging the free and uncritical use of drugs in general,” the committee believes, and there is also a need to counteract recent pro-drug propaganda.

As far as treatment for drug dependence is concerned, the committee believes that the British system of maintenance, in which an addict is supplied with daily doses of heroin, and the methadone maintenance treatment widely used in the United States both have their advantages and drawbacks. But a valid comparison between the two approaches cannot be made because of differences in the sociocultural environments and in the practice of medicine in the two countries. Both systems, however, share some success in limiting the obtaining of illicit drug supplies by the patient, and the committee points out that since the introduction of this approach in Britain, new cases of heroin dependence have been appearing much less frequently.

BLACK ARROW

Launch Postponed

A SECOND attempt to launch a British satellite with the Black Arrow rocket has been put back by about three months. Originally planned for late spring this year, the launch has been postponed to late summer—probably September—chiefly because of the fault in the second stage of the rocket which resulted in failure to launch a satellite last September. The next launch attempt will, however, still take place with the X3 satellite, as planned before the last failure. The Ministry of Aviation Supply, which is now responsible for the Black Arrow project, has therefore decided to risk a firing with a satellite worth about £2 million instead of making further inroads into the stock of rockets on order by repeating the September firing.

The Ministry is still, however, being coy about precisely what happened to the second stage of the rocket last September. But it seems that the fault was in the pressurization of the second stage oxidant tank; this caused the engine to stop 13 seconds too soon, and the third stage could not take the satellite into orbit. Luckily, the fault seems to have been relatively minor and little design modification will be necessary.

The X3 satellite will be essentially a technological satellite designed to test solar cells, thermal surfaces and a data handling system developed at Farnborough, but it will also carry a micro-meteorite experiment from the University of Birmingham. As for plans to launch

further satellites, little can be said at present. The budget for the Black Arrow project, which was set at about £3 million last year, rising to about £5 million in future years, is unlikely to escape entirely unscathed by the government's cuts in public expenditure. As one scientist said last week, the project “is being torn up by the roots every few months to see if it is still growing”.

ARCHAEOLOGY

“Rescue” to the Rescue

MANY of the hundreds of historic sites presently at risk in Britain could be saved if proposals put forward by a recently formed archaeological association are adopted. Launched at what may have been the largest meeting of professional and amateur archaeologists ever held in Britain and appropriately christened “Rescue”, the association aims to prevent the unwitting destruction of ancient sites by operations such as deep ploughing, afforestation and quarrying or urban developments such as the construction of new towns, airports and motorways.

The organizers of “Rescue” aim to achieve their objective in two ways: by raising funds through subscriptions, appeals and donations which can be used to finance full time central and regional administration, and by providing a source of informed and authoritative advice which could give town and country planners some idea of the archaeological risk involved in projected development schemes.

The need for such a campaign has been clear to archaeologists for many years, but the urgency has become apparent only recently. The present rate of destruction is appalling; some twenty to thirty deserted medieval villages are lost each year, and of 450 recorded Bronze age burial mounds in Gloucestershire, only one group remains intact. Although the amount of money which the government makes available for the preservation of historic sites has increased almost ten-fold in the last decade, the Walsh report, published late last year (Cmd 3904), concluded that the resources available are quite inadequate to cope with the problem. Finance alone is no solution, however, as Professor G. W. Dimbleby of the Institute of Archaeology, London University, emphasized last week. He felt that archaeological rescue operations frequently fall short of their potential. Too often archaeological items only are conserved and little thought is given to environmental aspects.

A strong element of realism runs through “Rescue's” thinking on conservation. It claims to be campaigning not for the wholesale preservation of ancient sites, nor seeking needlessly to obstruct urban progress, but it is asking for the

chance to survey possible sites before their irrevocable destruction, and the opportunity to preserve those sites of special importance. A message from Mr Peter Walker, Secretary of State for the Environment, which was read at the meeting and which expressed strong sympathy with "Rescue's" aims indicates, perhaps, that their call will not go unheeded.

INDUSTRIAL RESEARCH

Rise and Fall of BCURA

SIR JOHN EDEN, Minister for Industry, recently praised the work of the British Coal Utilization Research Association, pointing out that its "rate of growth as a contract research organization has been impressive", and that its prospects seem "excellent". But the National Coal Board evidently does not share that opinion, because it announced last week that BCURA is to be closed down. The NCB intends to withdraw its financial support from BCURA and, because the board is the only industrial member of the research association, BCURA will die from lack of funds.

The chief reason for the closure is that the National Coal Board has decided to concentrate its research activities at the Coal Research Establishment at Stoke Orchard, near Cheltenham. Some of BCURA's units and facilities will therefore be transferred lock, stock and barrel, while others will be closed down. A few of the association's 130 or so staff, who were informed only last week that the establishment is to close by the summer, will also be offered jobs at Stoke Orchard. On the face of things, the decision to concentrate resources seems sensible, but there are a few rather surprising aspects. Last October, BCURA opened a Materials Characterization Unit—it was this development which provided the platform for Sir John Eden to praise the establishment—and this is one of the units which will be transferred to Stoke Orchard.

The reason why the Materials Characterization Unit was not established at Stoke Orchard in the first place probably lies in the peculiar constitutional position of BCURA during the past two years. BCURA was established in 1938 as a government supported research association, but because the National Coal Board eventually became the dominant industrial member, it was decided in 1968 that the government's grant would be run down, and that the NCB should take the establishment over as a wholly owned subsidiary. Consequently, all the industrial members of BCURA, except for the NCB, resigned on December 31, 1968, and rejoined as associate members, and the NCB took over full

responsibility for BCURA on January 1 this year. The Materials Characterization Unit was therefore established before the NCB had complete control over the affairs of BCURA, although the coal board was the chief party involved in the planning of the establishment.

Over the past few years, BCURA has been building up its contract research, and it is estimated that the contracts this year would have brought in about £150,000 compared with about £80,000 last year. But the annual expenditure on the BCURA laboratories is about £800,000 and it seems that the NCB has decided that BCURA's income from contracts would have been unlikely ever significantly to reduce the financial burden on the NCB. As for the outstanding contracts which BCURA holds, the NCB is hoping that those which cannot be cancelled will be completed by the summer.

CHEMICALS

Shell Rethinks

THE Shell group of companies seems to be feeling the full effects of inflation. During the past week the company announced that work is to stop temporarily on the expansion of the Carrington chemicals complex near Manchester and Stanlow oil refinery at Ellesmere Port, Cheshire, while a reappraisal of the cost of the whole project is carried out.

The original plans were laid down about eighteen months ago and at that time the cost was estimated to be about £225 million, of which £150 million was earmarked for the Carrington project. Some of the Carrington plant was expected to be in operation by 1972 and completion was planned for 1975. Shell Chemicals UK Ltd and Shell UK Ltd now estimate that the total cost may be inflated by as much as 40 per cent.

The situation is considerably aggravated by the abolition of investment grants announced by the government at the end of last year and their replacement by investment allowances. Excessive inflation within the UK deals a second blow to the chemical industry under an investment allowance scheme because the international nature of the industry (and particularly of the Shell group) means that prices in Britain must keep in step with those elsewhere. Profits inevitably fall, and only a steadily reducing proportion of the overall investment in, say, the Carrington and Stanlow projects can be recouped from taxation. The result is a cash flow problem in one of the most capital intensive industries in the UK—the chemical industry utilizes 15 per cent of industrial assets but only employs about 5 per cent of the total industrial labour force.

Parliament in Britain

Food Contamination

MR JAMES PRIOR, Minister of Agriculture, announced that he has instituted a scheme for monitoring certain heavy metals in canned and fresh fish, and other foods important in the national diet. The Laboratory of the Government Chemist, the Government Fisheries Laboratories and the Plant Pathology Laboratory will analyse a primary sample of about 3,000 items a year. This will be supplemented by tests carried out by local authority analysts.

Methyl mercury will be the chief metal under consideration initially, but the pharmacology subcommittee of the Committee on Medical Aspects of Food Policy will later advise the Ministry of Agriculture on other heavy metals to look out for. The results obtained from the monitoring will be collated by scientists at the Ministry of Agriculture, and published at half-yearly intervals. They will also be submitted to the pharmacology subcommittee of the Food Additives and Contaminants Committee.

Special checks of the level of mercury compounds in food will also be made in areas in which local pollution may be abnormally high. (Oral answers, January 19.)

Radioactive Fallout

ALTHOUGH fission products from nuclear tests were detected in rainwater in Britain in 1969 and the first half of 1970, deposition was insufficient to cause detectable levels of ^{131}I in milk. There was also little change in the total deposit of ^{90}Sr and ^{137}Ce in the first half of 1969 and the corresponding period of 1970. This information was given by Mr Anthony Royle, Under Secretary of State, Foreign and Commonwealth Office. He also said that the fallout from the recent nuclear tests was small compared with that from the tests in 1962–63, and that the government will make no representations to France and China about the abandonment of nuclear bomb tests. (Written answers, January 25.)

ESRO

THE government's policy towards the European Space Research Organization was the subject of questions from Mr Tam Dalyell to Mr Frederick Corfield, Minister of Aviation Supply, and Mrs Margaret Thatcher, Secretary of State for Education and Science. Mrs Thatcher said that the government's policy remains unchanged, but it may have to be altered if the French and Danish governments carry out their intentions to secede from ESRO. Mr Corfield said that despite doubts in some European countries about the future of ESRO, the British government has no intention of withdrawing its support from the organization. (Written and oral answers, January 20.)

NEW WORLD

Nixon buys Plan for Attack on Cancer

by our Washington Correspondent

In announcing last week to Congress that he would request an additional \$100 million for cancer research, President Nixon seems to have come close to accepting a plan to set up a NASA-style agency charged with conquering cancer by the same methods used to put men on the Moon. Put forward less than two months ago by a group working outside the usual channels of the scientific advisory apparatus, the plan calls for the National Cancer Institute to be set up as a separate agency outside the National Institutes of Health and endowed with an initial annual budget of \$400 million.

In his State of the Union message last week President Nixon did not refer specifically to the proposal to set up a separate cancer agency, saying only that he would ask in his budget for the financial year starting this July for an extra \$100 million "to launch an intensive campaign to find a cure for cancer". He added that he would ask later for whatever additional funds could effectively be used, since "the time has come when the same kind of concentrated effort that split the atom and took man to the Moon should be turned toward conquering this dread disease. Let us make a total national commitment to achieve this goal", the President said. "America has long been the wealthiest nation in the world. Now it is time we became the healthiest nation."

The request for an extra \$100 million would increase by half the present budget of the National Cancer Institute, raising it much of the way towards the \$400 million target proposed by the panel of consultants to the Senate Committee on Labor and Public Welfare in its report on December 4 last year (see *Nature*, 228, 1133; 1970). Another echo of the panel's report in the State of the Union message is Mr Nixon's comparison of cancer research to the Apollo programme, an analogy which many scientists would regard as of limited truth but which was a major selling point of the Senate panel's report.

The Senate panel's proposal for a blitz on cancer has met with a certain lack of enthusiasm among non-medical scientists, partly because at a time when research funds of all kinds are scarce it was feared that an extra allocation for cancer could only be made at the expense of other fields of research. This objection may fade if, as is reported, the President's budget proposals due to be announced later this week hold increases for scientific research far better than had been expected. Even so, many will remain unconvinced that so much extra money can be

spent on cancer research without duplicating or triplicating work in a field that is already overcrowded, particularly in its most promising areas such as virology and immunology. For example the Special Virus Cancer Programme administered by the National Cancer Institute received an extra \$25 million from Congress last year and an official of the programme said recently he was not having to turn away good ideas for lack of funds.

It is not yet known by what channel the idea of an intensive campaign against cancer reached Mr Nixon's attention. Dr Edward David, the president's science adviser, was consulted on the proposal, as was the Secretary of Health, Education and Welfare, and both apparently recommended it. The initiative, however, seems more likely to have come from one or other of the Senate panel members, several of whom have close connexions with the Nixon administration. The 26-man panel includes Mr Elmer Bobst, chairman of the Warner-Lambert pharmaceutical company, who is a close friend of Mr Nixon's. Mr Benno Schmidt, the chairman of the panel, is well known to the director of the Office of Management and Budget, Mr George Schultz, and a third member of the panel, Dr Lee Clark of the M. D. Anderson cancer institute in Houston is a friend of Mr John Connally, the new Secretary of the Treasury. In addition Mr Schmidt and Mr Laurance S. Rockefeller, also a panel member, are heavy contributors to the Republican party funds.

Whether or not Mr Nixon's request is in response to the Senate panel's proposal, those connected with the panel report are encouraged by the unexpected turn of events. Mrs Mary Lasker, a New York millionairess who is credited with considerable influence in winning Senate sponsorship of the resolution setting up the panel, said this week that she was delighted with the President's commitment to cancer research. Mr Robert E. Sweek, a staff consultant to the panel whose experience in the planning of applied research could command a prominent role in the proposed cancer agency, is also pleased with the way things are going, although, like Mrs Lasker, he denies knowledge of whether Mr Nixon has the panel's programme in mind.

Whether or not Mr Nixon intends to set up a separate cancer agency will remain unclear probably until his message on health affairs expected next month.

Whatever the President's exact intentions, the Senate panel proposal has

another influential ally in Senator Edward Kennedy who recently gained the chairmanship of the Health Subcommittee of the Senate Committee on Labor and Public Welfare. Kennedy made clear during the last session of Congress that he would introduce legislation to implement the Senate panel's proposals if he gained the chairmanship.

A distinctive feature of the new approach to cancer envisaged by the Senate panel's report is the systematic planning of research of the type that has been successful in applied research projects such as the Polaris submarine and Apollo programmes. The panel's report calls for a national crusade against cancer to proceed by four chief avenues of approach—elimination of chemical and other carcinogens, improved screening methods and the earlier detection of cancer, making present methods of cancer treatment more widely available and, fourthly, doing more research. The panel was chaired by Benno C. Schmidt, managing partner of the New York company of J. H. Whitney, and Dr Sidney Farber, director of the Boston Children's Hospital, served as co-chairman.

GOVERNMENT

Advice to Advisers

by our Washington Correspondent

At a cautious estimate there now exist some 2,000 expert scientific committees advising federal government on technical matters ranging from the efficacy of anti-submarine devices to the safety of food additives. The invitation to serve on one of these committees is not easily turned down as it offers the chance of influencing events as well as of serving the nation. But those who follow the profession of science adviser, according to a recent study prepared at Stanford University, risk having their advice suppressed or distorted by government, their confidential knowledge turned as a weapon against outside critics, and their prestige used as an aura to hallow the government's action even when it runs directly contrary to the advice tendered. To remedy such abuses, the Stanford study proposes that the scientist accepting an advisory position should be bound by a set of guidelines to express his doubts in the open if he sees public welfare endangered by government policies of which he has expert knowledge.

Based on a set of seven case studies in which abuses of this sort are said to have

occurred, the Stanford report* concludes that science advisers are valued not just for the quality of their advice but also to give the appearance of legitimacy to political decisions—"An adviser often finds himself playing the role of high priest whose ministrations during the preparation of a policy are supposed to make the policy immune from political attack." The report, which is the product of a year-long student-faculty workshop at Stanford, describes, in language more colourful than usual for academic prose instances of "disturbing reports which have leaked through cracks in the strict wall of secrecy with which the administration has surrounded its advisers". These include a report by the AEC's Advisory Committee on Reactor Safeguards which in 1956 declined to guarantee the safety of a nuclear power plant at Lagoona Beach, Michigan (the report was suppressed, the reactor suffered a serious meltdown); the report of an Ad Hoc Review Committee set up by President Nixon in 1969 to review the SST programme (the committee concluded that the noise of the aircraft would be intolerable but the programme went ahead nevertheless); a report by the President's Science Advisory Committee expressing concern about the dangers of triggering off earthquakes with underground nuclear explosions (the report was suppressed for nearly a year during which the Atomic Energy Commission implied the committee's findings had been reassuring); reports by panels of the National Research Council on the safety of cyclamates which recommended on four occasions that use of the sweeteners should be controlled (the Food and Drug Administration persistently ignored the advice); and other reports on the efficacy of the anti-ballistic missile system, hazards of DDT and the possibility of teratogenic effects caused by the herbicide 2,4,5-T.

The authors of the Stanford study are two physicists, Frank von Hippel, now at the Argonne National Laboratory, and Joel Primack, now at Harvard University. Their interpretation of the cases they have studied is that a science adviser should accept that his primary responsibility is not to the person or agencies he is advising, as in a lawyer-client relationship, but to the nation as a whole. Other guidelines offered for consideration are that an adviser should speak out when he believes information is being needlessly withheld and public debate hampered, and should make public the areas on which he is advising and the general nature of the information to which he has access. Another guideline bids an adviser to give on request to responsible opposition groups whatever

information he legally can, "including his opinion on whether any secret information of which he is aware vitiates their arguments".

SANTA BARBARA

Oil Damage Surveyed

by our Washington Correspondent

THE Santa Barbara oil spill of January 1969, often cited in the same breath as the Torrey Canyon disaster as an exemplary technological insult to the environment, may not be entirely worthy of its place in contemporary ecological folklore. According to an 18-month survey of the biological aftermath of the spill, the damage to the fauna and flora in the Santa Barbara Channel was much less than had been predicted and was often hard to distinguish from other influences.

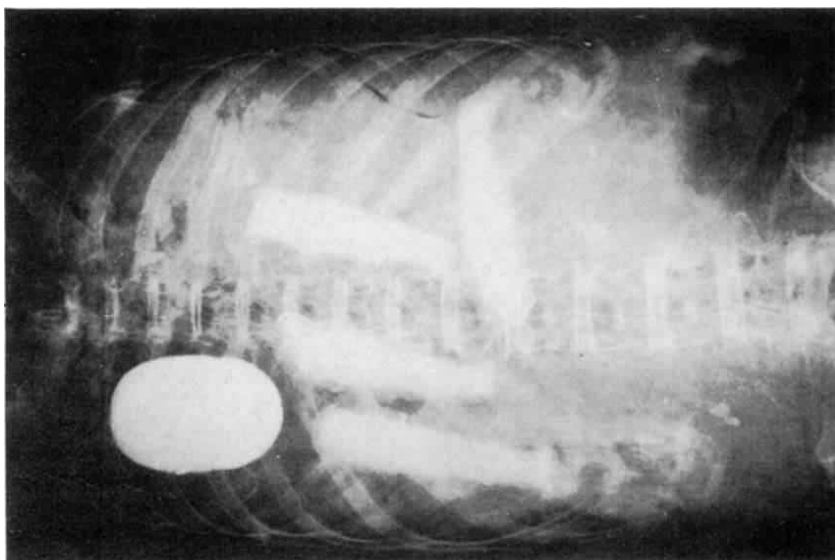
The bulk of the oil, amounting to perhaps a million tons, escaped after one of the wells of an offshore drilling platform ran out of control. The well was cemented 11 days after the blow-out, but further oil continued to escape from the site of a former natural seepage apparently reactivated by the drilling operations. A study carried out by a 20-man team based at the Allan Hancock Foundation of the University of Southern California attributes rather slight damage to the oil spill, the only serious casualties being sea birds and a species of barnacle, *Chthamalus fissus*. Other kinds of marine life may have been harmed to a lesser degree

but minor effects are hard to assess because of lack of precise knowledge about the situation before the spill.

A preliminary report of the findings prepared by Dr Dale Straughan states that there was "very little mortality" in the Santa Barbara area due directly to the oil probably because the more toxic fractions are also the most volatile and disappear after a few days of floating on the open sea. Mortality among the barnacle species *C. fissus* was probably caused by the animals being physically smothered by the oil rather than by chemical effects. The fish catch in Santa Barbara Harbor was lower than usual during the six months after the spill but the commercial catch for the wider area including the Santa Barbara Channel and the Channel Islands was no different from the same period in 1968. There is no evidence of damage to plankton and no evidence definitely attributable to the spill of damage to benthic organisms. A survey of sandy beaches during the year following the spill failed to pinpoint any damage from pollution. But some 4,000 birds, mostly pelagic species, died during the two months after the blow-out.

Full results of the study are to be published soon in book form. The study was financed by grants to the Allan Hancock Foundation of \$242,000 from the Western Oil and Gas Association and \$12,000 from the Sea Grant Programme. The Western Oil and Gas Association, Dr Straughan said last week, attached on conditions to the use of its money.

Ribcage Treasures



A large heart scarab and four Sons of Horus statues revealed inside the ribcage of Queen Notmet (circa 1080 BC), wife of King Herihor. The jewellery was revealed in the course of an X-ray examination of 29 mummies in the Cairo museum by Dr James E. Harris and a group from the University of Michigan. Other jewellery, covered by resin or inserted into the body cage so as to escape the attention of grave robbers, was found on the mummies of Seti I, Thutmose III and Amenophis I. The objects are said to be the first royal Egyptian jewellery to be discovered since the opening of Tutankhamen's tomb in 1922.

* *The Politics of Technology*. By Frank von Hippel and Joel Primack. Copies obtainable from SWOPSI, 590A Old Union, Stanford University, Stanford, California 94305. Price \$7.50.

Astronomy in Chile

In the past few years the Chilean Andes have become the chief centre for observational astronomy in the southern hemisphere. But during recent months astronomers' excitement at the possibilities given by the clear skies of the Andes has been tempered by the sober considerations of international politics.

If and when present plans mature, Chile will have an even greater concentration of large optical telescopes than California. Major observatories are being constructed by at least five foreign groups—the European Southern Observatory (ESO), the Carnegie Institution of Washington (CARSO), the Cerro Tololo Inter-American Observatory (CTIO) operated by the US National Observatory based at Kitt Peak, Arizona, the David Dunlap Observatory operated by the University of Toronto, and finally, a Soviet observatory.

Three of the groups are basing their activities on mountains in the foothills of the Andes within 50 miles of the town of La Serena which lies on the coast about 300 miles north of Santiago. The European consortium of France, Germany, Holland, Belgium, Sweden and Denmark (which Britain refused to join several years ago) already has several small telescopes on their mountain, La Silla. This station is directed by Dr Bengt Westerlind, the well-known Swedish astronomer who worked for several years at the Mount Stromlo Observatory in Australia and who has made important contributions to the study of the Magellanic Clouds and the structure of the southern Milky Way. A 140-inch telescope is now under construction for this observatory.

A few miles from La Silla is Las Campanas, the mountain which has been selected by CARSO (which in the northern hemisphere runs the Mount Wilson Observatory as a joint operation with the Palomar Observatory of the California Institute of Technology), and a forty-inch telescope is being constructed there. An ingenious optical system will enable the telescope to photograph fields about 3 degrees in diameter down to magnitude 22—this will be of particular value in studies of the large and small Magellanic Clouds, which are each about 5 degrees in extent.

The Carnegie Institution has made strenuous attempts in recent years to fund a 200-inch telescope for its CARSO station. The latest attempt, a joint proposal with the National Research Council of Canada to the Canadian government, was recently withdrawn, chiefly, it seems, because of disagreement among Canadian astronomers about the

advantages of a Chilean site compared with Mount Kobau in British Columbia. Despite this setback the fact that the trustees of the Carnegie Institution have committed themselves to the expense of developing such a remote site points to their determination to make Las Campanas into a major observatory.

The third group near La Serena is the Inter-American Observatory on Cerro Tololo, directed by Dr Victor Blanco. At present this is the largest of the observatories in Chile. Two 16-inch telescopes, a 36-inch and a 60-inch telescope are in routine use by a staff of about six young astronomers and by a steady stream of visitors from the United States. The building and dome for a new 150-inch telescope is nearing completion on Cerro Tololo. It is expected that the telescope and mirror will be ready in two or three years' time. A small Soviet station is on Cerro Catan, nearer the bright lights of Santiago than the western astronomers' mountains.

What has led to the activity in Chile? There are three potentially good areas in the southern hemisphere: South America, Australia and South Africa. Of these, Australia has the worst sites. The best sites for astronomical observatories are usually found on mountains 6,000–8,000 feet high around latitudes 30 degrees north or south. Australia has no high mountains at this latitude and although it has a dry climate, the cloud cover seems to be on average higher than other continents.

On the other hand, there are excellent sites in South Africa—although Cape Town, which houses the southern branch of the Royal Greenwich Observatory, and Pretoria, which is the site of the 74-inch telescope now operated jointly by the Radcliffe trustees and the Science Research Council, are not good. The Cape is too low and has mediocre seeing, and the sky at Pretoria is too bright for much important work on faint objects. Moreover, the cloudy season in Pretoria occurs during the southern summer when the Magellanic Clouds—one of the chief reasons for observing in the southern hemisphere—are overhead. These factors, together with the British decision to join with the Australians in building a 150-inch telescope in New South Wales, has led to the recent plan to concentrate the South African telescopes at a site near Sutherland in the Karoo.

The sites in the Chilean Andes are all excellent. They enjoy remarkably long periods of "photometric" sky conditions and the size of the seeing disk under the best conditions is already an astronomical legend. It is likely that equally good

conditions can be found in South Africa and no doubt one of the considerations which influenced the Europeans, for example, to go to Chile was the internal policies of the present South African government.

Politics has, however, now entered the astronomy scene in Chile. The recent election of Dr Allende's Marxist government, with its declared policy of nationalizing foreign-owned businesses, must be a source of concern to the astronomical groups, particularly the Americans. But there is no doubt that the astronomers are an asset to Chile. Their activities are innocent and they occupy land which is otherwise useless. Moreover, all the groups have arrangements whereby Chilean astronomers have access to the telescopes for a fraction of the time. If this opportunity is used wisely it will enable a relatively poor country like Chile to have a leading place in one of the most exciting fields in modern science.

There is little danger, however, that the Chileans will nationalize telescopes. It is understood that representatives of both CARSO and CTIO have talked with Dr Allende since his election and have been assured that their presence is welcomed by his government. A more dangerous threat to the plans for large telescopes in Chile lies, however, in the attitude of the US government which may well refuse to go ahead if the large American investment in Chilean industry is lost.

That is why this week's announcement that the Carnegie Institution will be building a 100-inch telescope at Las Campanas is good news. It will be built with a gift from Mr and Mrs Crawford H. Greenewalt of Wilmington, Delaware, in memory of Mrs Greenewalt's father, Irénée du Pont, which will be supplemented with funds from the institution and elsewhere.

The telescope itself will have a long focal length of 730 inches combined with a large field of focus about twenty times that of the 200-inch Hale telescope. A broad complement of instrumentation to go with the telescope is already being planned by the Carnegie Institution, and a great deal of the control of the telescope is going to be automated.

The David Dunlap Observatory of the University of Toronto is also to build at Las Campanas by agreement with the Carnegie Institution and the University of Chile in Santiago. The Canadian telescope is comparatively modest, however—a 24-inch reflector—but its capabilities will be boosted by the quality of the site and the instrumentation that will also be provided.

NEWS AND VIEWS

Is the Bubble Bursting?

IN more than one quarter during the past six months, as laboratory after laboratory hastened onto the bandwagon, hopes that it might be possible to exploit the discovery of reverse transcriptase(s) in the diagnosis and possibly even treatment of cancer have been running very high indeed. Little more than six weeks ago, for example, Spiegelman, at a lecture at the Royal College of Surgeons (see *Nature*, **228**, 1255; 1970), reported to an expectant audience that his group had detected enzyme activities, capable of transcribing double stranded DNA from single stranded RNA templates, not only in animal tumour viruses but also in white blood cells of some forty patients suffering from leukaemia and two biopsies of human osteosarcomas. By contrast they had failed completely to detect this activity in comparable cells from normal human blood and from patients with non-malignant blood diseases. Gallo *et al.* had earlier reported essentially similar but far less extensive findings (*Nature*, **228**, 927; 1970), and there was a widespread feeling that an assay for reverse transcriptase might, at the very least, prove to be a useful tool for diagnosing malignancy and following the course of remissions and relapses during, for example, the chemotherapy of leukaemia. And the more sanguine optimists were talking of new approaches to cancer chemotherapy, such as the design of antimetabolites specific for reverse transcriptase and therefore malignant cells, and at last tracking down human cancer viruses. Experiments reported in last week's and this issue of *Nature* and elsewhere are, however, likely to cause at least a temporary recession among such speculators; there are enough warning signs to suggest that the bullish market is fast heading for a slump. Reverse transcriptases are neither unique to established cancer viruses nor to cancer viruses and malignant cells; they are present in other RNA virus and apparently normal cells.

Last week Stone and his colleagues reported in *Nature* (**229**, 257; 1971) that visna virus particles, which have a structure and composition similar to the RNA tumour viruses, contain reverse transcriptase. Identical findings have also recently been reported by Lin and Thormar (*J. Virology*, **6**, 702; 1970) and by Spiegelman's group (*Proc. US Nat. Acad. Sci.*, **68**, 182; 1971). And Parks *et al.* also reported in *Nature* last week (**229**, 259; 1971) that they had detected reverse transcriptase in primate syncytium-forming (foamy) virus, the particles of which also closely resemble those of the RNA tumour viruses. Neither foamy virus nor visna virus are known to be associated with tumours; visna virus causes a slowly progressing neurological disease of sheep and the pathogenicity of the primate and related foamy viruses of other species has yet to be determined. Clearly either these two classes of viruses have hitherto unsuspected oncogenic potentials or reverse transcriptases are not uniquely confined to cancer viruses.

And if this activity is not unique to cancer viruses, the question of whether it might occur in normal as well as malignant cells naturally arises. The experiments reported by Scolnick, Aaronson, Todaro and Parks, on page 318 of this issue, suggest that reverse transcriptase does indeed

occur in normal cells, or at least in murine and human cells in tissue culture, which show no evidence of being infected by a tumour virus.

Scolnick *et al.* apparently set out to discover whether, by using synthetic RNA or DNA-RNA hybrids as template, which Spiegelman has shown greatly increases the sensitivity of reverse transcriptase assays, it is possible to detect activity in cells transformed by a tumour virus or infected with a foamy virus. With poly rA·rU as template they detected activity in crude extracts of murine BALB/3T3 cells transformed by murine sarcoma virus and monkey kidney cells infected with primate foamy virus. There was no activity in comparable extracts of untransformed BALB/3T3 cells or uninfected monkey kidney cells. But when the synthetic RNA-DNA hybrid poly rA·dT was used as template, extracts of both the infected and control, uninfected cells showed reverse transcriptase activity even though the uninfected cells are not malignant. This unexpected result raised the possibility that other cells, which are neither malignant nor overtly infected with any known virus, in other words other types of normal cells, may contain reverse transcriptases.

Scolnick prepared crude extracts of cultured normal diploid fibroblasts, derived from skin biopsies of normal subjects and maintained in culture for not more than five transfers, cultures of lymphocytes from healthy individuals and malignant lymphocytes straight from patients with acute leukaemia and tested them in the assay with poly rA·dT. All were positive although the amounts of activity in these extracts were less than in cells producing a tumour or foamy virus. Further, the activity detected varied with the amount of protein, a measure of the amount of extract, used in the assay, all other components being constant. As a result Scolnick and his colleagues decided to partially purify the activity before comparing the template specificities and sensitivity to N-demethylrifampicin of reverse transcriptase in normal and malignant cells. After partial purification, and it is only partial, the activities irrespective of their sources were found to be remarkably similar, showing the same template preferences and sensitivity to the drug, which is known to inhibit the RNA dependent DNA polymerase in animal tumour virus particles. It would, of course, be premature to say that the enzyme in virus infected or cancer cells is the same as that in normal cells, without having completely purified and characterized the enzyme from various sources. Nevertheless, the findings of Scolnick and his colleagues raise many extremely important questions and have many implications.

They shed doubt on the idea that an assay for reverse transcriptase is likely, in the near future, to become a diagnostic tool for cancer. Had the enzyme been restricted to malignant cells or cells infected with tumour viruses, a qualitative, all or none assay would have been feasible. But now reverse transcriptase activity has been detected in normal, albeit cultivated, cells any diagnostic assay must be quantitative rather than qualitative. And developing such an assay depends on a far more detailed understanding of the enzyme and factors such as cell division rate,

and state of differentiation for these may affect the expression of reverse transcriptase in non-malignant cells. At present it is not obvious why Spiegelman and his colleagues have repeatedly failed to detect the activity in normal white blood cells, but the observation that the activity detected in crude extracts depends on the protein concentrations in the assays may have something to do with it. Furthermore, it now seems clear that anti-metabolites specific for reverse transcriptases will not be specific for malignant cells—a great disappointment.

Aside from the cancer problem, the discovery of reverse transcriptases in some non-malignant, apparently normal cells has many implications for molecular and cell biology. Assuming that the normal cells Scolnick *et al.* used were not accidentally infected with a tumour or foamy virus during their period in culture, which seems extremely unlikely, the reverse transcriptase which they contain must

have been specified by a genetic element in the cells, either a latent and vertically transmitted virus or some cellular gene. In these days of oncogenes (putative cellular genes capable of causing a cell to go malignant and of becoming part of a tumour virus) and proviruses (putative cellular messenger RNAs which together with reverse transcriptase may escape a cell and, being infectious, transfer their genetic information to another cell), the distinctions between the genome of a cell and of some of the viruses which infect that cell are fast vanishing, in theory at least. Both the oncogenic and provirus hypotheses postulate that tumour viruses are escaped cellular genetic elements, and such a ferment of revolutionary ideas cries out for rigorous experimental testing. In particular we need to know in detail the comparative biochemistry of reverse transcriptases purified from various sources.

Ring out the Old, Ring in the New

It comes as quite a shock to realize that, only ten years ago, the paper by Drs Dietz and Holden which appears on page 309 of this issue of *Nature* would have been regarded as a joke. Speculation on the existence of pre-Mesozoic ocean floor would, at that time, have been a bit like asking whether there is any sand in the desert, and would have been dismissed with the sort of contempt normally reserved for those ancient philosophers who wrangled at length on the question of angels on pin points. For such is the revolution that has taken place in the Earth sciences over the past decade that the oceans, once the oldest and most mysterious part of the Earth, now appear as young features with comparatively simple geology and with histories far less complex than that represented by the contortions of the continents more than 3,500 million years ago.

It is easy to see, in retrospect, that the reason why the oceans were what they were to the old geologists was largely a matter of ignorance. Of course, in the broad sense the reason for any wrong idea is ignorance; but in the case of the oceans, the point has a particular relevance. For the oceans were at least as old as the continents not because this was a postulate or necessary consequence of some all-embracing global theory of Earth behaviour, but only because there was no reason to suppose otherwise. In short, the ocean floors were thousands of millions of years old by default—there was simply no reason to think that the sort of tectonic process which has been a feature of continental history should not also be typical of the oceanic crust. If there was an alternative view at all, it was only that tectonic activity in the ocean floor might have been less frequent than on the continents. Few thought of the possibility that the oceans might be susceptible to vastly different forms of tectonic activity.

Thus it was that the lack of any large scale horizontal movement in the continental crust was, perhaps understandably, carried over to the ocean floors with little refinement. If detailed bathymetric surveys of the ocean floor had been available, the obsession with vertical movement may not have lasted quite so long. As it was, in ignorance of the true situation the oceans became the receptacle for all sorts of problems which could not be

solved in any other way. For instance, to explain the distribution of similar flora and fauna between continents separated by vast stretches of sea, it was necessary to invoke the unlikely concept of land bridges—narrow strips of dry land which once spanned oceans but which, having served their avowed purpose, sank out of sight. As long as there was no way of detecting sunken land bridges, this theory of vertical land movement served its purpose well enough. But once the veil of factual ignorance had been removed, the vertical limitation was revealed for the *ad hoc* assumption it was.

And so the picture of the oceans began to change. Long before the so-called revolution of the 1960s, the young science of seismology had begun to reveal the oceans as sites of peculiar activity; and it soon became apparent that, devastating though earthquakes in inhabited continental areas might be, the oceans were far more prone to seismic activity. Then, in the later 1950s, the first comprehensive bathymetric charts of the ocean floors showed that, far from there being sunken land bridges, the most impressive topographic features were the mid-oceanic ridges which combine to form practically a continuous system tens of thousands of miles long. From this it was but a short step to correlating mid-oceanic ridges with the sites of the majority of the world's earthquake epicentres.

But satisfying though the new vision of the oceans may be from the purely academic point of view, the new global tectonics has its practical disappointments. Today, the oceans are often regarded as the great blue hope for solving the world food problem; but it is easy to forget that not so very long ago the ocean floor was also regarded as a vast potential mineral El Dorado.

Whether, as Dietz and Holden imply, possible pre-Mesozoic ocean floor offers the prospect of useful minerals whose retrieval is economically viable remains to be seen. And whether, as they suggest, the Wharton Basin in the Indian Ocean is just such pre-Mesozoic crust remains to be tested directly. What is certain is that historians of the future will have much more fun charting the events which transformed the pre-Mesozoic from the old young to the new old.

MEMBRANES

Protein Patterns

from our Molecular Biology Correspondent

Most of what biochemists learn at their mother's knee relates to the behaviour of biologically active molecules in aqueous solution. When confronted therefore with materials that are insoluble in water, and that reside and function in a condensed non-aqueous phase, they are apt to react with a baffled resentment, which explains perhaps the faltering touch so evident in much published work on the proteins of membranes. So far as red cell membranes are concerned, it is now apparent that the greatest cause of confusion has been the failure of relatively drastic treatments to achieve complete disaggregation, with consequent appearance of various associated forms in fractionation profiles. Lenard (*Biochemistry*, 9, 5037; 1970) has taken advantage of the hard-won knowledge, that treatment with detergent at 100° C leads apparently to complete disaggregation, to compare the proteins from the red cells of five mammalian species, including man. It is now clear that the protein patterns in gel electrophoresis are in fact very similar, and that there are eight principal protein fractions in all cases, the largest of which have molecular weights of about 250,000. The pattern of labelling with a radioactive thiol reagent is also the same in all cases, with 50 per cent of the label in the high-molecular weight components. One prominent component in each membrane is a glycoprotein.

The search for the loci of specific activities in membranes has been assisted by the design of affinity labels. Kiefer *et al.* (*Proc. US Nat. Acad. Sci.*, 67, 1688; 1970) have performed an affinity-labelling exercise on the acetylcholinesterase of red cells, as well as the acetylcholine receptor site of the neuromuscular junction in intact muscle. They have used a refinement of the method, whereby the reactivity of the label is triggered photochemically. The quaternary ammonium analogue of acetylcholine is attached to an aromatic azide. This can be photolysed to yield a highly reactive excited nitrene, which is expected to react with a variety of side chains. The advantages in this development are considerable: in the first place the binding properties of the ligand can be measured before irradiation. Second, non-specific reaction at points remote from the ligand site can be almost completely eliminated, because of the rapid decay of the excited species, assisted if need be by added scavengers in the buffer. It is only then the bound ligand that reacts with the protein within the lifetime of the active state. Kiefer *et al.* suggest that it may be possible to localize active sites by irradiation of a tissue in the presence of a label with a fine laser beam.

An altogether simpler system than the red cell, in terms at least of the multiplicity

of constituents, is the retinal rod outer segment, which contains a stack of flat membrane bags, containing rhodopsin as effectively the sole, or at least predominant, protein. It therefore requires no very daring flight of the imagination to conjecture that the bleaching of the rhodopsin, which is already known to be accompanied by some kind of conformational adjustment, causes excitation by way of a change in the membrane permeability and thus a flux of ions. Now Heller, Ostwald and Bok (*Biochemistry*, 9, 4884; 1970) have demonstrated that some such effect can indeed occur. The membranes, it is reported, are not permeable to alkali and alkaline earth ions, and when the osmotic pressure of the surrounding medium is changed they pick up or lose water to maintain osmotic balance. By recovering the particles from a suspension and weighing them, any volume changes can then be determined. Heller *et al.* find that whereas in the dark the volume remains almost constant, illumination in the presence of ATP and of sodium, potassium and calcium chlorides results in slow volume change of some 15 per cent, or 25 per cent of the interstitial space within the membranes. The membranes still maintain an ionic balance, however, which indicates that this is not simply a matter of leakage. Calcium chloride and ATP are both involved in mediating the change.

Though it cannot be denied that this is an interesting result, it must be recognized that its relation to the visual excitation process is not yet obvious: in the first place the volume change is slow, and furthermore it occurs at 4° C but not at 30° C. The suggestion of Heller *et al.* is that a change in membrane structure causes a change in passive transport of sodium and potassium against which the ATP-dependent pump has to work. The change is manifested only at 4° C when the pump velocity is diminished. This, however, is not easy to reconcile with the enhancing effect of ATP on the volume change.

MARINE BIOLOGY

Tuna, Starfish and Kelp

from a Correspondent

THE chief theme of the Challenger Society's meeting at the British Museum (Natural History) on January 13 and 14 was on the development of fisheries especially in African countries. The Challenger Society exists to promote the study of oceanography, but from time to time it has taken an interest in the ecology and fishery problems of the great lakes of Africa. The special lecture by Dr D. N. F. Hall (Overseas Development Administration, Foreign and Commonwealth Office) on the British aid programme to tropica

Control of Haemoglobin Synthesis

LITTLE is known about how the amount of protein synthesized by an active gene is controlled in higher organisms. The synthesis of haemoglobin is a particularly good system to use for investigating this problem, because haemoglobin is a direct gene product which is made in considerable quantity by reticulocyte cells, which can be readily obtained. Two studies on haemoglobin synthesis by Esan *et al.* and Nute and Stamatoyannopoulos, which will be published in next Wednesday's issue of *Nature New Biology*, were directed to this end.

Esan's group used human subjects who are heterozygous for the beta chain of haemoglobin. Such individuals must possess one gene which codes for a normal beta chain and one copy of its allele representing the mutant form. But the haemoglobin which they synthesize contains more of the normal than of the mutant type chain.

One explanation for this discrimination would be that wild type chains might be preferentially synthesized, either because mutant mRNA is unstable, or because it is translated more slowly or less frequently. Because reticulocytes possess no DNA and therefore cannot synthesize RNA, following protein synthesis shows directly what is happening

to the translation of mRNA. When Esan *et al.* incubated reticulocytes with radioactive amino-acids, the haemoglobin produced followed the usual overall chain proportions; if differential production of protein were responsible for the mutation, the abnormal ratios of mutant to wild type chains would have been exaggerated. Esan *et al.* suggest therefore that the explanation for the selection may be that the alpha chain of haemoglobin prefers to associate with a normal beta chain rather than an aberrant one.

Human γ -haemoglobin is of more than one type (Schroeder *et al.*, *Proc. US Nat. Acad. Sci.*, 60, 537; 1968), and each type seems to be coded by a separate gene. Nute and Stamatoyannopoulos have followed up this finding by looking at the haemoglobin of Macaque monkeys with electrophoresis on urea gels and analysis of peptide digests. They show that these monkeys seem to have at least two loci which code for the γ -haemoglobin polypeptide chain; this implies that one mechanism which cells may use to control the quantitative synthesis of proteins is the utilization of more than one gene to code for it. But it seems likely at present that this sort of mechanism is restricted to systems such as haemoglobin synthesis.

fisheries biology set the scene and was followed by three lectures on aspects of freshwater fisheries biology.

The first day's second session on the seas restored the balance for the oceanographers present. Mr N. R. Merrett (National Institute of Oceanography) gave a summary of the work conducted at the East African Marine Fisheries Research Organization by himself and his predecessor on an experimental fishery for tuna and billfish (marlins, spearfish, and the like). The fishing method adopted was that used by the very successful Japanese floating long-lines modified to suit the available equipment. Considerable stocks of both tuna and billfish were found offshore of the Zanzibar station, and although migration and seasonal conditions caused local fluctuations in the species present there were sufficient stocks all the year. The survey catches, however, averaged about half of the Japanese average catch of 2.8 pounds per hook, a figure which may be partly attributable to the higher efficiency of the Japanese crews and vessels. The problem therefore was whether the potential catch available to local boats could make a viable fishery, and Merrett thinks that it may be possible in view of the closeness of the fishing areas to the East African coast. Certainly these fishes could make a contribution to the tourist industry of the region if treated as sport fish. Merrett pointed out, however, that here, as elsewhere, the catch has fallen considerably in the past four years probably as a result of overexploitation.

Dr R. F. G. Ormond (Physiological Laboratory, University of Cambridge) reported the studies by two Cambridge expeditions of the coral-eating starfish *Acanthaster planci* in the Red Sea. In this region it has not been reported in the plague quantities that it has assumed in Guam and parts of the Great Barrier Reef, and for this reason it offers opportunity to study the animal under more or less normal conditions. In the vicinity of Port Sudan an average population of from one to four specimens per kilometre of reef was found, but it was noticed that *Acanthaster* does not favour either shallow still waters, or exposed reefs where wave motion is pronounced. It seems to be most common under conditions of moderate exposure and where the coral cover is complete. *Acanthaster* is known to be attracted to areas where coral has been damaged, but in this area of the Red Sea little underwater blasting has taken place. In spite of the valuable contributions that these expeditions have made to a better understanding of this starfish we seem to be no nearer to evaluating the causes of the local plagues. Indeed, the discussion following Ormond's contribution revealed a body of opinion in favour of the hypothesis that these population explosions are normal, if irregular, events in the biology of the

starfish, which biologists have not previously been able to observe, and which have never before generated such interest.

The fauna of the kelp in the sublittoral along the north-east coast of England was discussed by Dr P. G. Moore (Wellcome Marine Laboratory, Robin Hood's Bay). Collections from fifteen sites over the single tidal periods had resulted in the identification of some 90,000 animals representing 387 species in the holdfasts of the kelp. This work is part of an overall investigation into the kelp flora of the north-east coast especially in relation to pollution. Moore's work, however, suggests that the local turbidity of the water is a more important factor affecting the variety of the kelp fauna than is pollution.

SCAMPI

Harvest of the Loch

In spite of its importance to fishermen and gourmets, remarkably little is known about the biology of the animal which provides scampi. In 1970 Scottish fisheries yielded 8,000 tonnes of *Nephrops norvegicus*, worth £2 million. It is the tail of this animal, also known as the Dublin Bay prawn although it is really a

close relative of the common lobster, which constitutes scampi. *Nephrops* also forms the basis of other important



Nephrops norvegicus in a burrow.

fisheries off the coasts of north-western Europe, and so it is hardly surprising that two biologists have been studying the ecology and behaviour of this animal for three years, as members of the Linnean Society learnt at their meeting on January 14.

One puzzle for fishermen has been the variation in the size of catches. And so one of the first aims of Dr C. J. Chapman (Marine Laboratory, Torry, Aberdeen) and Dr A. L. Rice (British Museum (Natural History)) was to investigate the burrowing habits of *Nephrops*, and dis-

Transmuting a Virus

WHEN inoculated into hamsters mouse sarcoma virus can induce tumours, the cells of which, either immediately or after passages in other hamsters, yield a sarcoma virus which is specific for the hamster. How is this change in the host range of a sarcoma virus brought about? In next Wednesday's *Nature New Biology* Kelloff and his colleagues report experiments which indicate that simply growing mouse sarcoma virus in hamster cells in culture is not sufficient to transmute the virus into a hamster specific particle. All their evidence points to the conclusion that the conversion of a mouse sarcoma virus into a hamster sarcoma virus depends on the presence in the hamster cells of the so-called hamster "leukaemia" virus, which, acting as helper, provides the mouse sarcoma genome with the internal proteins and envelope of a hamster virus.

Hamster "leukaemia" virus was itself first identified in a virus preparation obtained from a hamster tumour induced by murine sarcoma virus. As far as is known this virus cannot induce sarcomas, neither has it been proven that it can in fact cause leukaemia in hamsters but by other criteria it seems to be analogous to the mouse leukaemia viruses. Presumably this virus is not present in the cultures

of hamster cells in which Kelloff and his co-workers propagated various mouse sarcoma viruses; as a result the viruses obtained from these cells retain all the essential characteristics of a mouse virus. On the other hand the animals which carried tumours induced by the mouse virus but yielding a hamster sarcoma virus presumably harboured hamster "leukaemia" virus, which provided the parts necessary to change the specificity of the sarcoma genome.

Clearly, growing a sarcoma virus of one species in the cells of a second is not sufficient to change the host range of that virus. But if the cells of the second species carry genetic information which can specify a tumour virus, envelope transmutation may occur. This finding and similar observations made on other cell and virus combinations should serve as a caution to those who propagate animal tumour viruses in human cells in culture. There is a real possibility that some human cells might contain either a dormant or defective virus or other genetic information sufficient to provide an animal tumour virus genome with an envelope with a specificity for human cells. And, conversely, the animal virus might provide components which render infectious a defective human tumour virus.

cover whether individuals spend much of their time hidden in the mud safe from the fishing nets. They dived in the relatively shallow water of Loch Torridon, on the west coast of Scotland, to count *Nephrops* and its burrows, and tracked animals moving out of their burrows by recording their footprints on small trays of 'Vaseline' placed outside the entrances. The form of some burrows was investigated by the preparation of casts from polyester resins. This technique was carried out with considerable success, and Rice had several casts, about one metre across, with him at the meeting.

In 1969 the density of burrows in ninety square metres of mud was recorded as 1/1.4 m², and there was one *Nephrops* in every 5.5 m². The animals, apparently, had no permanent homes, sometimes moving rapidly from burrow to burrow and sometimes staying in one place for a longer time. It was clear that in the relatively shallow water of Loch Torridon, *Nephrops* tends to stay hidden away during the day, coming out during the night. This is reminiscent of trawl catches which are generally greater during the night in shallow water.

The situation was quite different in the deeper water of the Sound of Jura, also on the west coast of Scotland. Chapman's data, collected with an underwater television camera towed under a research vessel, show that *Nephrops* was much more active during the day than during the night. Rice thinks that light intensity is the cause of this difference in burrowing behaviour. He suggested that *Nephrops* has an optimum range in which it can be active, so that in deep water light intensity is too low at night and in shallow water it is too high during the day.

If this seems to have solved one problem, there is still the mystery of the apparent absence of young *Nephrops*. Although in three years Rice and Chapman have seen only adults, with a carapace more than 30 mm long, the young ones must be somewhere in both Loch Torridon and the Sound of Jura. They hope to find them yet.

SEMICONDUCTORS

Evidence for Bonding

from our Solid State Physics Correspondent
AN upsurge of interest in the chemical or bonding characteristics of semiconductors has followed the work of J. C. Phillips (*Phys. Rev. Lett.*, **20**, 550; 1969) and others in which the key to a better understanding of the chemical and physical properties of semiconductors and insulators was held to lie in a detailed knowledge of the distribution of the electronic charge inside the solid. Accurate calculations of band structure have already been carried out but little effort has been made to reproduce the electron charge

density in these materials to an equivalent accuracy.

J. P. Walter and M. L. Cohen of the University of California at Berkeley (*Phys. Rev. Lett.*, **26**, 17; 1971) have now evaluated the charge density contours for the valence electrons in germanium, gallium arsenide and four other crystalline materials and have discovered that the nature of the bonding is clearly portrayed by these contours. More significantly, the calculations have provided direct support for the notion that structures of four-fold coordination with covalent bonding can be differentiated neatly from six-fold structures held together by electrostatic forces by the value of the ionicity parameter as defined by Phillips and Van Vechten.

This idea had been arrived at previously only on empirical grounds.

Walter and Cohen computed the electronic charge from wave functions derived in calculations of pseudopotential band structure. Up to ninety plane waves were needed to represent the wave functions. Several striking features appear in the contours of charge density: for germanium, for example, the tetrahedral covalent bonding can be seen clearly from the concentration of electronic charge halfway between adjacent atoms. The greater ionic character of GaAs can be detected from the shift of the centre of the bonding charge away from the halfway position towards the As atoms. The total amount of bonding charge also gets less in going from Ge to

Unusual Ribosomes of Mitochondria

MITOCHONDRIA possess both their own genetic apparatus and the machinery of protein biosynthesis, and there is much current interest in the characteristics of these structures within these little organelles. This is reflected by the appearance of a batch of three articles in next Wednesday's *Nature New Biology* dealing with mitochondrial ribosomes.

Brega and Vesco and Attardi and Ojala have studied the structures involved in the biosynthesis of proteins within mitochondria from the human cell line HeLa, and have found three types of ribonucleoprotein particles present within the mitochondria, with sedimentation coefficients of 55–60S, 40–45S and 30–35S. These workers prove beyond doubt that the heaviest particles are single ribosomes, and that the two lighter classes are the two types of ribosomal sub-particles, containing RNAs of 16S and 12S size. Both the ribosomes and their constituent RNAs are, of course, remarkably small compared with cytoplasmic ribosomal particles of either eukaryotic or prokaryotic cells, and similar findings have already been reported for ribosomes from the mitochondria of other types of animal cells.

The structures active in protein synthesis within intact mitochondria have been found to be polysomes containing several 55–60S ribosomes, and Brega and Vesco have isolated polysomes with sedimentation coefficients as large as 200S. The considerable technical difficulties involved in demonstrating this were overcome by inhibiting cytoplasmic protein synthesis specifically with the cytotoxic drugs pederine or cycloheximide, which do not interfere with mitochondrial protein synthesis. Proteins synthesized in the presence of these drugs were labelled by using radioactive amino-acids as precursors. Labelled polysomes were then obtained from isolated mitochondria by dissolving them with detergent. But

addition of chloramphenicol, which is known to specifically block mitochondrial protein synthesis, prevented the formation of labelled polysomes. Puromycin causes the disappearance of radioactivity from both the monosome and polysome fractions, presumably by releasing the nascent polypeptide chains.

Attardi and Ojala present an interesting speculation about the evolution of mitochondrial ribosomal RNA. They point out that the ribosomal RNAs of animal cell mitochondria are considerably smaller than those of mitochondria from lower eukaryotic cells, and that a parallel decrease in the size of mitochondrial DNA has also occurred. The mitochondrial DNA of animal cells is usually about 5μ in length, and they suggest that this is a lower size limit, representing the minimum amount of information necessary for mitochondrial function. They postulate that the reduction in size of the ribosomal cistrons was a part of the overall diminution of the mitochondrial genome during evolution.

In a third article, Lizardi and Luck reveal that mitochondrial ribosomes from *Neurospora* lack a 5S RNA, previously thought to be a universal constituent of ribosomes. They took the essential precaution of preparing material entirely uncontaminated by cytoplasmic ribosomes, by isolating the mitochondria by isopycnic centrifugation through sucrose gradients. Electrophoresis of RNA from whole mitochondria, or from extracted ribosomes and polysomes, shows that no 7S or 5S RNA components are present and Lizardi and Luck thus rule out that the RNA is likely to be leached out of the ribosomes in the course of extraction. Even more conclusively, they find that labelled RNA synthesized by isolated mitochondria does not contain either of these components (although short pulses yield 5S-like material which they postulate to be tRNA precursor molecules).

GaAs, indicating the changing balance from predominantly covalent to predominantly ionic character.

The ionicity parameter of Phillips and Van Vechten is a function of various energy levels in the crystal, and varies from zero to unity in going from fully covalent to fully ionic bonding. Phillips (*Rev. Mod. Phys.*, **42**, 317; 1970) noticed that for sixty-eight binary crystals, a value of 0.785 neatly separated the more covalent four-fold coordinated crystals of the structure of wurzite or zinc blende from the more ionic crystals of the rocksalt structure. This value was arrived at without any theoretical justification for a sharp division. Walter and Cohen have surmised that the change of crystal structure comes about as the covalent bonding vanishes, the limits of the bonding charge being defined from the position of the outermost closed contour. They have therefore plotted values for this charge against ionicity for two series of crystals, Ge, GaAs and ZnSe in the fourth period of the periodic table and α -Sn, InSb and CdTe in the fifth period. The values for the ionicity at zero bonding charge were 0.79 and 0.78 respectively, in excellent agreement with Phillips's figure. Thus the notion of a well defined ionicity as the threshold between structures of different coordination and bonding can be seen to have some basis in the model of pseudopotential band theory.

drilled, however, to a depth of 35 m fifteen years ago in an unsuccessful attempt to develop geothermal power in a known geothermal area. The upper 17.7 m of the hole is in alluvial fill below which lies 2.1 m of water-bearing sand. The rest of the hole is drilled into solid lava. The interesting thing about this otherwise undistinguished well is, however, that every 8–10 h it erupts to a height of 30–40 m and continues to erupt for about a minute each time. Each chief eruption is then followed a few minutes later by a second, lesser outburst, and occasionally by a third.

Why does this well erupt at all? From a series of temperature profiles down the well at various times throughout the eruption cycle, Rinehart has been able to piece together the events leading to an eruption. An hour or so after the previous eruption, the temperature at every point in the well lies below the boiling point curve, but not everywhere by an equal interval. At about 7.5 m from the top the temperature is less than 1° C from boiling; but in other places the temperature difference may be anything up to 30–40° C. As time goes on, the water at the 7.5 m depth boils. Steam bubbles rise in the well but are quickly condensed by the cooler water above, which is warmed as a result. Because of

the flashing of water into steam at the 7.5 m level the temperature there is lowered, but soon rises again to produce another flash. In other words, at this point the temperature periodically rises above and falls below the boiling point. While all this is going on, the water in the upper 7.5 m circulates in the pipe but the water below remains steady.

As the process proceeds, the water in the lower part of the pipe begins to heat up. Immediately before an eruption there is a second temperature peak at about 18–19 m, which would seem to indicate that heat is being supplied through the thin porous sand layer possibly in the form of hot water. Finally, there comes a point when the water above 7.5 m is no longer able to absorb the heat from the rising bubbles. The steam then suddenly blows off the head of superheated water. This is the observed eruption.

Why there should be a second eruption soon after the first is not quite clear. Rinehart found it impossible to measure the temperature profile between the two eruptions because of the short time interval involved. But what probably happens is that the hot water from below which replaces the ejected water enters a preheated pipe and rapidly reaches the unstable situation.

GEYSERS

Man-made Eruptions

from our Geomagnetism Correspondent

So many Earth scientists today work with a perpetual image of seafloor spreading at the backs of their minds that it is good to be reminded, once in a while, that there are other things in geophysical life besides the new global tectonics. Take geysers, for instance: the 1,728-page *Dictionary of Geophysics* apparently contains not one reference to it. Nobody imagines, of course, that the study of geyser action is going to bring about any sort of revolution in the Earth sciences; but it would be a great pity if this and other lesser-known phenomena were to receive no attention at all. Fortunately, this is not the case. J. S. Rinehart, for example, has been investigating the thermal and seismic properties of geysers for many years, having made a special study of America's most famous example, the Old Faithful geyser in Yellowstone National Park.

Rinehart (*J. Geophys. Res.*, **75**, 6714; 1970) has now turned his attention to an artificial geyser, Crump well, in Lake County, Oregon. It may come as something of a revelation to learn that there is such a thing as a man-made geyser at all. The 15 cm diameter Crump well was

Problem of Excess X-rays Eased

HARD on the heels of the MIT survey of the X-ray sources in the direction of the galactic centre (*Nature*, **229**, 96; 1971), Pounds's group at Leicester is this week publishing its survey of an adjacent area of sky between galactic latitudes 310° and 220°. The Leicester group is making a speciality of this region, which corresponds to the southern hemisphere constellations Norma, Lupus and Centaurus. The group's latest article—in next Monday's *Nature Physical Science*—reports data from a Skylark rocket flight in April 1969, and comparison with a similar experiment a year earlier (reported by Cooke, Griffiths and Pounds, *Nature*, **224**, 134; 1969) shows that some of the sources can be counted among the X-ray variables. This is the classification that was opened with the appearance in 1967 and subsequent decay of Cen X-2, which the second Leicester flight shows to be still faintly detectable in spite of previous evidence to the contrary. As well as Cen X-2, the sources Cen X-3 and Lup X-1 seem to be variable according to the comparison and were more intense during the second flight.

Altogether seven sources are covered in the survey which was sensitive to energies between 1 and 12 keV, and including those mentioned already the

sources whose strengths are given are Nor X-1 and X-2 and Cen X-1 and X-5. Cen X-5 is a new source, not recognized before, which is below the sensitivity levels of earlier surveys.

The Leicester group has been particularly concerned with a background flux of X-rays coming from the plane of the galaxy which on the face of it is not attributable to identifiable point sources. Such an excess of X-radiation, coming from the Centaurus–Carina–Vela area, was recognized in the 1968 flight and several mechanisms were put forward—suprathermal proton bremsstrahlung, electron capture from neutral hydrogen by heavy nuclei in cosmic rays, inverse Compton scattering of starlight or the blackbody radiation, or simply unresolved sources along the galactic equator that are below the sensitivity threshold.

With the data from the second Leicester flight to play with, the situation now looks much simpler. When the sources Cen X-1, X-2, X-3 and X-5 that appear in the data from the second flight but which were not unambiguously resolved in 1968 are allowed for in the 1968 data, only ten per cent of the excess background flux is left unaccounted for, in the Centaurus region at least.

METALLURGY

Artefact Analyses

from our Archaeology Correspondent

THERE has been much effort recently toward the realization of a dream of prehistoric archaeologists—the determination, by the analysis of copper and bronze artefacts, of the source from which the constituent metal came. A successful solution to this problem would bring much useful information concerning early trade and the beginnings of metallurgy. But it now seems that the attainment of this goal is further away than ever, and that most of the data painstakingly accumulated may be of little value.

The underlying idea is that individual ore bodies are characterized by particular combinations of trace elements, so that analysis of early artefacts will repeat their characteristic “fingerprint”. (Obviously this could work only for the early period, before the extensive remelting of used objects led to the mixing of copper from different sources.) There have been many analyses of the composition of the trace elements of different ore types from various localities. For example, following earlier analyses by Otto and Witter and by Neuninger and Pittioni, a Stuttgart group has divided thousands of objects, on the basis of the concentrations of various trace elements, into groups which supposedly reflect the place of origin of the metal (S. Junghans, E. Sangmeister and M. Schröder, *Studien zu den Anfängen der Metallurgie*, 1, 1960 and 2, 1968).

The efficacy of the statistical method (H. Klein, *Ber. Röm.-Germ. Komm.*, 34, 103; 1951) used by this team to group these analyses was always open to question because of its reliance on successive elements taken in turn. A much more persuasive average-link cluster analysis of the type now familiar in biological taxonomy has been carried out by F. R. Hodson (*World Archaeol.*, 1, 90; 1969) who divided a hundred objects into sixteen groups on the basis of the Stuttgart analyses. Some individual groups have a wide geographical distribution, however, and a feature of the method is that all the elements considered are given equal weight.

J. A. Charles and E. A. Slater (*Antiquity*, 44, 207; 1970) now question whether the Stuttgart analyses are repeatable to the level of accuracy used in their classificatory procedure. They show that segregation on cooling can cause very considerable variation in the concentrations of elements in different parts of the same object—up to 30 per cent in the case of bismuth. Because bismuth ranks prominently among the five elements used to effect the original classification into groups, the criticism is a damaging one. It reflects much less on Hodson's pro-

cedure because this is a multivariate analysis, without yes/no decisions determined by the concentration of a single element.

Ultimately, however, the statistician and the metallurgist must face the problem presented by the ore bodies themselves. In how many cases can the ores of a given region be expected to yield metal which (1) regularly conforms to its supposed trace element “fingerprint”, and (2) is not duplicated in composition by ores elsewhere? Clearly the first step must be a statistical consideration of different types of ores, of the kind begun by Friedman and his colleagues (*Science*, 152, 1504; 1966). Unfortunately it seems that the confidence levels for such statements may not be very high, and the archaeologist may be left to choose between the metallurgical “probability”

that two objects found at opposite ends of Europe originated from the same ore and the archaeological “probability” that they did nothing of the sort.

The position does indeed look gloomy. The director of the Research Laboratory for Archaeology at the University of Oxford expressed a pessimistic view at a recent symposium (E. T. Hall in *The Impact of the Natural Sciences on Archaeology* (edit. by T. E. Allibone), Oxford University Press, 1970): “Our experience at Oxford has tended to show that such analyses are a waste of time. . . . It is technological improvements in manufacturing technique which can be demonstrated by analysis of the major constituents of bronzes rather than the solution of attribution problems by trace analysis”. Unfortunately, it seems that Hall may be right.

Galactic Helium from Massive Stars

FOR some time it has been believed that there is a maximum mass of about one hundred solar masses for stars. Above that mass, theoretical calculations predict that the stars are unstable and that the instability occurs rapidly compared with the evolution of the star. Recently, nonlinear calculations by several authors have suggested that the instability is significantly stabilized at large amplitudes and that the stars only lose mass at a rate comparable with that at which hydrogen is converted into helium by nuclear reactions inside them. If this is so, a considerable amount of helium could be produced in such stars and be expelled.

Talbot and Arnett suggest in next Monday's *Nature Physical Science* that this could be an important source of helium in our galaxy, although they admit that their estimates of helium production are rather crude at present. If this is so, there must have been a first generation of very massive stars when our galaxy was formed and detailed calculations would need to show that the stars have lost most of their mass after helium has been produced but before substantial production of heavy elements, which seem to be about ten times less abundant by mass than helium in young stars.

There is particular interest in the subject of helium in the universe because helium is the only element which is comparable in abundance with hydrogen in the part of the universe which we can observe directly. Recently it has been popular to suppose that the originally created matter consisted only of light elements and that the heavier elements have been built up by nuclear fusion reactions, probably inside stars. The crucial question is

whether the matter which was originally created was hydrogen alone or a mixture of hydrogen and helium.

A few years ago it was found that all objects, for which reasonably reliable helium abundances existed, possessed at least 25 per cent of helium by mass. It was then realized that the hot big bang cosmological theory propounded by George Gamow predicted that nuclear reactions should have produced a mixture of hydrogen and helium after the first few minutes of the expansion of the universe, which could be regarded as the initial chemical composition of the universe. At that stage it was impossible to predict a precise amount of helium, but the discovery of the microwave background radiation changed the situation (A. E. Penzias and R. W. Wilson, *Astrophys. J.*, 142, 419; 1965). The hot big bang theory requires the universe to be filled today with a blackbody distribution of microwaves and the temperature of the radiation determines the initial helium production. The temperature of about 2.7 K predicted a helium content close to 25 per cent (R. V. Wagoner *et al.*, *Astrophys. J.*, 148, 3; 1967).

Although this theory of primaeval helium production is very attractive, it cannot be valid if objects are discovered with little or no helium or if the microwave radiation proves not to be of blackbody form when all the relevant wavelengths have been studied. There have recently been observations which suggest both of these results. Although the primaeval origin of most of the helium has certainly not yet been disproved, it seems desirable to consider other possible origins of helium and this is what Talbot and Arnett have now done.

INTERFACES

Phase Energies

from our Materials Science Correspondent

As men living at the interface of the earth and air, as scientists living at the interface of the prosaic and the mysterious, as travellers scowling at customs men, we cannot escape interfaces. Certainly the detailed description of interfaces has been a sustained concern of scientists of many kinds; materials scientists, for instance, have long studied the morphology, composition and energies of interfaces between crystals or between phases. An exact knowledge of interfacial energies, in particular, is a precondition of understanding the behaviour of interfaces in systems undergoing transitions, and a particularly important category of transition is the homogeneous nucleation and growth of a stable phase at the expense of a metastable one.

According to Volmer, Becker and Döring's classical theory of homogeneous nucleation, an embryo of the stable phase becomes viable and grows steadily only when, by a chance fluctuation, it comes to exceed a critical spherical size. This size is such that a further atom, in deserting the metastable for the stable phase, releases in volume free energy more than the interfacial energy needed for the nucleus to increase in size. The theory has long been accepted as a central tenet of the theory of phase transformation (and of freezing of liquids in particular), but it has never been rigorously confirmed by experiment. The nearest approach, perhaps, was an attempt by Sundquist and Oriani in 1962 to relate critical undercooling in a two-liquid miscibility gap to the known interfacial energy. Subsequent criticism, however, casts doubt on the reliability of their conclusions. A. E. Nielsen and S. Sarig (*J. Cryst. Growth*, **8**, 1; 1971) have now published results, obtained by means of an ingenious technique, which really seem to constitute a quantitative confirmation of the Volmer-Becker-Döring theory. They studied nucleation of droplets of second phase in a ternary miscibility gap in the methanol-water-tribromomethane system. Two liquids were mixed rapidly and completely at a rapid flow rate, and the time τ to onset of turbidity was measured to a factor of a millisecond. This delay time constitutes an induction period for droplet nucleation plus diffusion controlled growth to a size large enough to scatter light to a detectable degree. Because the supersaturation of the mixed liquid is known, and the volume fraction of new phase is small enough to have negligible effect on the composition of the parent liquid, all terms are known in the Volmer equations except the interfacial energy σ : thus σ can be calculated from the measured τ

values for different compositions and supersaturations of the parent phase. Nielsen and Sarig compared these σ values with values measured directly by means of the classical drop weight method and obtained good agreement for the two sets of σ values, subject to a correction made for the variation of σ with surface curvature for very small droplets. This agreement was obtained for delay times less than 1 ms, corresponding to large supersaturations. Longer times corresponded to anomalous behaviour which Nielsen and Sarig attribute to heterogeneous nucleation.

Interfacial energies in another context have been considered by G. H. Bishop, W. H. Harth and G. A. Bruggeman (*Acta Metall.*, **19**, 37; 1971). These

workers have examined the morphology of grain boundaries in zinc bicrystals of controlled orientations, and have found that for certain narrow ranges of misorientation (close to but not identical with twin orientations) the boundary became stably faceted—that is it did not strive to achieve a state of minimum total area. The nature of the “energy cusps” in the Wulff plot, which expresses grain boundary energy as a function of grain boundary orientation for a fixed mutual orientation of the contiguous lattices, was analysed in detail from the observed boundary morphologies: the determination of these cusps is an important achievement at a time when interest in grain boundary structure has suddenly revived after a long period of quiescence.

Radio Prediction of Solar Proton Events

A SOLAR flare heralds a violent outburst of energy from the Sun which produces radiation extending from radio wavelengths, through optical, to X-radiation as well as high energy protons and slower moving plasma clouds. The X-rays and microwave bursts reach the Earth almost simultaneously with the light, but the more energetic protons arrive after times ranging from a few tens of minutes to several hours. The low energy protons and the plasma cloud reach the Earth and interact with the upper atmosphere 1 or 2 days later still. D. L. Croom has been investigating methods of predicting these solar proton events and he reports his findings in next Monday's *Nature Physical Science*.

The study of the proton streams associated with solar flares is important for two principal reasons. First, these relatively rare events are little understood. It is known, for example, that relativistic protons with energies between 1 and 60 GeV actually reach the surface of the Earth and that lower energy protons of from 30–300 MeV can penetrate into the ionosphere at the poles and produce absorption of radio communications. But much more information is needed about the phenomena which are so effective in accelerating particles to these high energies and the mechanisms which can contain both high and low energy protons in the solar corona and the interplanetary medium for such a wide range of times. Clearly some warning of the onset of such events would be a great advantage in preparing equipment, particularly the launching of balloons and rockets for the detection of the less energetic particles high in the Earth's atmosphere.

The second reason for interest is that these proton events may have an effect on man. The most intense solar proton events reaching the Earth's surface may

exceed the constant galactic background cosmic ray level by a factor of up to ten for a few tens of minutes; this will have an integrated effect on the surface of the Earth which adds little to cosmic ray dose received by man. But outside the Earth's protective atmosphere the effects of the flux of lower energy protons which lasts much longer and occurs more frequently cannot be dismissed so readily. Plans for manned space flight, and particularly extravehicular activity on the Moon and planets, must obviously include some precautionary avoiding action; similar steps may be necessary for high level flying in aircraft such as Concorde. Any warning of such a proton event which can be given by optical or radio observations is therefore highly desirable.

For about 10 years it has been known that a particular kind of radio emission associated with solar flares, known as type IV activity, is connected with proton events. This activity is a continuum which can extend right through the radio spectrum from decametre to millimetre wavelengths and is caused by synchrotron emission from electrons emitted at the time of the ejection of the high energy protons. Although all proton events are associated with type IV activity, the reverse is not true—not all type IV events are followed by proton events and they are therefore not a reliable guide. Croom now claims to have found a more reliable method of predicting solar proton events using detailed spectral characteristics of type IV events. Following up ideas put forward by Castelli, Aarons and Michael (*J. Geophys. Res.*, **72**, 5491; 1967), Croom has found that centimetre and millimetre wave observations are critical in setting up criteria for distinguishing proton and non-proton associated type IV events.

Recent Developments in X-ray Astronomy

by

K. A. POUNDS

Department of Physics, University of Leicester

In the past two years notable advances have been made in X-ray astronomy. The first X-ray pulsar has been discovered, several variable sources have been observed, and more X-ray sources have been identified with optical and radio objects. This article by Dr Pounds of the Leicester group reviews the progress that has been made.

IN the period since Friedman's review¹ in this journal the number of known cosmic X-ray sources has steadily increased and is now near fifty. The first high resolution spectroscopic and polarization studies have been reported—though with negative results in each case. On the other hand, the first X-ray pulsar has been discovered, further highly variable sources observed and several important new identifications made. Recent observations below 1 keV have indicated the probability of numerous bright sources and an excess diffuse X-ray component in this previously unexplored spectral region. The aim of this article is to review these more recent developments in cosmic X-ray astronomy and perhaps also set the scene for the significant changes in the observational situation that are likely to follow the introduction of major satellite instruments over the next few years, as outlined in the final section.

Astronomically, the X-ray data on a particular source assume real importance when that source has been identified with a known optical or radio counterpart. Only then can the distance and hence the absolute flux of X-rays be estimated and the implications on the physical nature of the particular star, supernova remnant, radio galaxy, or whatever, be examined. At present reliable identifications exist for six galactic supernova remnants (the Crab Nebula, Tycho Brahe's nova, Cas A, Cygnus Loop, Vela X and Puppis A), a thirteenth magnitude flickering blue star (Sco X-1), two of the three brightest known radio galaxies (Virgo A and Cen A), and the optically brightest quasar (3C 273). In addition to this formidable array of key objects, the X-ray source Cyg X-2 has been linked with reasonable certainty² with a fifteenth magnitude (binary?) star and a weak X-ray signal has been reported³ from our nearest neighbouring galaxy, the large Magellanic Cloud.

The Crab Nebula

Probably the most remarkable recent X-ray measurements have been those obtained on the Crab Nebula, first identified as an extended X-ray source in 1964. In Friedman's article it was noted that a major problem lay in explaining the continuing flux of X-rays, believed to be of synchrotron origin, when the responsible 10^{13} – 10^{14} eV electrons would radiate away their energy in a few months. About the time of publication, towards the end of 1968, a pulsating radio source (NP 0532) was discovered inside the Crab Nebula. Very quickly there followed the observation of correlated pulses at both optical⁴ and X-ray wavelengths^{5,6}. Apparently the pulsar

itself was capable of accelerating electrons to the required energies for synchrotron X-ray emission. As models for the pulsar NP 0532 have developed, generally invoking a neutron star spinning at the 33 millisecond pulsation period, an explanation of the Crab X-ray emission has emerged. Careful measurements have shown NP 0532 to be gradually slowing down, at a rate of 1 part in 2,000 per yr. The corresponding decrease in rotational energy, for a body of near solar mass and a diameter of several kilometres, is of the order of 10^{38} erg s⁻¹, a comfortable order of magnitude greater than the total Crab X-ray flux. Approximately 10 per cent of the X-radiation is contained in the pulses at 1–10 keV (ref. 6), increasing to 17 per cent near to 40 keV (ref. 7) and possibly to near 100 per cent above 600 keV, according to a balloon observation in August 1970 by the Bristol University group (unpublished work of R. R. Hillier *et al.*). The diffuse kilovolt X-ray source, extending over 1–2 arc min, corresponding to two light years or so at the distance of the Crab, may now be explained as a direct consequence of the life span of the high energy electrons leaking away from the vicinity of the pulsar.

Other Supernova X-ray Sources

As the remarkable detail of the Crab Nebula source has unfolded during the past two years, several other supernova remnants have been confirmed as powerful X-ray emitters. Early in 1969 the American Science and Engineering (ASE) group observed 1–10 keV X-rays from Cas A and Tycho Brahe's nova (SN 1572), the measured fluxes being respectively 0.1 and 0.04 of that of the Crab⁸. In neither case was the spectral detail sufficient to indicate a preferred thermal or synchrotron X-ray production mechanism. Pulsations were searched for in vain over a wide range of periods, from a few milliseconds to several seconds. Indeed, despite intensive searches, no optical or X-ray pulsed source other than NP 0532 has been detected so far. It appears once again that, in our Galaxy, the Crab Nebula is at present unique.

Within the past year X-ray sources have also been located in the Cygnus Loop and the Vela X/Puppis A supernova remnants. In each case the X-ray spectrum is notably softer than in most other known sources. The Cygnus source was first identified⁹ by the Livermore group who found it to be extended over 2° or 3°. In a later observation, in June 1970, the ASE group confirmed this identification (P. Gorenstein at the IAU assembly, Brighton, 1970) and found a spectrum consistent with a thermal source of 4 million degrees Kelvin. The Cygnus Loop, believed to be some 50,000 years old and 2,000 light years away, is one of the oldest and largest known supernova remnants and illustrates a probable later stage in the evolution of sources like the Crab Nebula and Cas A. The soft X-ray source in the Vela region has been examined by both the Livermore and Leicester University groups, the former identifying an extended region of X-ray emission with the Vela X and Puppis A remnants¹⁰ and the Leicester measurements (presented by B. A. Cooke and myself at Brighton) indicating again a thermal spectrum with a characteristic temperature of 4.5 million degrees K. Such temperatures are similar to those found in active regions of the solar corona and may well contain strong line emissions of elements such as neon, oxygen, nitrogen and carbon, an intriguing prospect for future spectroscopic studies.

Scorpius X-1

The first cosmic X-ray source to be detected, and still the brightest, Sco X-1, has continued to attract considerable attention during the past two years. There is now good evidence for slow, factor-of-two variations in both the spectral slope and intensity of the 1–10 keV X-rays (M. Oda at IAU symposium No. 41, Munich, 1970), and more rapid “flaring” on a time scale of tens of minutes, has also been reported^{11,12}. Balloon observations have shown a variable, hard spectral component, evident above 40 keV (ref. 13). There is also weak evidence for correspondence in the optical continuum and X-ray variations¹⁴. The “crucial” measurement to confirm the thermal nature of Sco X-1, by a search for X-ray line emission, has been carried out twice during 1970, in each case using a large-area Bragg crystal spectrometer flown on a stabilized rocket platform. In March the Leicester group was unable to detect an emission line of helium-like iron (reported by R. E. Griffiths at Brighton), expected to appear near 6.65 keV, and in the following month a team from Columbia University also failed to see an anticipated spectral line of highly ionized sulphur. The former result is perhaps the more interesting because careful analysis of previous proportional counter spectra by the Goddard Space Flight Center and Lockheed groups has indicated a positive “bump” in the spectrum near 6.5–7 keV (refs. 15 and 16). At present it seems that, despite the failure to see narrow emission lines, the Sco X-1 source is probably of a thermal nature. Observations in the optical and infrared have provided clear evidence¹⁷ for a high source opacity at these longer wavelengths and a compact ($\sim 10^9$ cm), high density ($\sim 10^{16}$ cm⁻³) plasma has been proposed. In such an object an X-ray photon would make on the order of a hundred collisions with fast-moving electrons in the source plasma before escaping, suffering Doppler shifts of 10 per cent or so on each occasion. Thus an emission line could be broadened to such an extent as to be unobservable with a high resolution spectrometer, and yet remain as a broad emission feature detectable with a proportional counter.

The nature of the Sco X-1 source remains largely a mystery. The compactness of the hot plasma cloud suggests that it is probably gravitationally confined and, as the thermal energy is radiated away in a fraction of a second, continuously replenished in some way. As pulsars, and therefore in all probability neutron stars too, appear to be rather numerous within the Galaxy, a likely model for Sco X-1 may involve the interaction of a neutron star with a dense cloud of gas, probably another star. There is now some evidence for a steady underlying decrease by about 10 per cent per year in the Sco X-1 kilovolt flux^{18,19} indicating that the X-ray source may have a life span measured in tens of years. If a binary star system is involved that was formed in very recent times, it seems necessary to suggest a chance collision of the two objects, because the recent creation of the neutron star would surely not have passed unnoticed and neither would it have left its partner star relatively undisturbed.

Highly Variable X-ray Sources

As well as the supernovae sources and X-ray stars of the Sco X-1 type, a third distinct class of galactic X-ray object is now emerging. The previous review article described a source, Cen X-2, which appeared early in 1967, was at one time comparable in brightness with Sco X-1, and then rapidly faded from view. In July 1969 a second short-lived source was observed, also in Centaurus and named Cen X-4. This object was discovered with proportional counters on board the US nuclear detection satellites Vela 5A and 5B, first appearing between July 6 and 9 and rapidly growing to 2.5 times the intensity of Sco X-1 (ref. 20). Thereafter, until mid-August the source decreased slowly, by a factor of two, and then faded quickly, finally to disappear (less than 0.5 per cent peak) on September 24. The crude spectral data available²¹ may be interpreted as a rapid cooling or expansion of the source over the first few days, followed by a long isothermal phase, with an effective tem-

perature of 45 million degrees K. The remarkable similarity of the time histories of Cen X-2 and Cen X-4 and of optical novae of the DQ Herculis type lends support to the idea that these X-ray sources involved the explosive ejection of stellar material. A downturn in the Cen X-4 spectrum below 4 keV requires strong absorption, corresponding to a column density of 3×10^{22} hydrogen atoms cm⁻². At the relatively high latitude ($b^{\text{II}} = 25^\circ$) of Cen X-4 the integrated interstellar gas amounts to only 10^{21} atom cm⁻² and it seems that the absorbing material is most likely to be in the form of a dense circumstellar cloud. This, incidentally, may also explain the failure to observe an optical counterpart to Cen X-4.

Several other galactic X-ray sources are undoubtedly strongly variable and recent Leicester data have indicated Lupus X-1 and Cen X-3 to be of this type. The latter source is also notable in having an unusual spectrum which does not fit the normal exponential or power law approximations. Instead, the spectrum peaks around 4 keV and falls rapidly to both higher and lower photon energies (reported by Cooke and Pounds, at Brighton). It seems to be the closest to an X-ray blackbody spectrum yet recorded. Undoubtedly, the study of such highly variable sources will be one of the most interesting aspects of the forthcoming satellite observations.

X-ray Galaxies and Quasars

Until recently Virgo X-1 was the only confirmed extragalactic X-ray source, having been identified²² with the massive elliptical galaxy M87 and associated radio source (Virgo A). The lack of other extragalactic X-ray objects was rather surprising, particularly in view of the intense, diffuse background radiation, which is almost certainly extragalactic and may well arise as the integrated effect of large numbers of radio galaxies, quasars, and so on. Now workers at the University of California, Berkeley, have reported²³ significant X-ray fluxes from the strong radio galaxy Cen A and the quasar 3C 273, observed during a gyro-stabilized Aerobee rocket flight in June 1969. The large-area proportional counters flown in this experiment also scanned across M87 and obtained signals for Cen A, M87 and 3C 273 of 0.04, 0.045 and 0.25 counts cm⁻² s⁻¹ respectively in the 0.25–12 keV band. With the accepted distances of these sources of 1.3×10^7 , 5×10^7 and 1.9×10^9 light years, respectively, the corresponding intrinsic X-ray powers are 5×10^{41} , 10^{43} and 1.5×10^{46} erg s⁻¹. These are all well in excess of the 10^{39} – 10^{40} erg s⁻¹ estimated to be the overall X-ray emission of our own Galaxy, but still fall well short of the fluxes required to explain the observed diffuse background in a simple manner, as discussed later. The X-ray power relative to emission at other wavelengths also indicates that all three are distinctly different types of X-ray source. Thus M87 at this flux level is dominantly an X-ray emitter, producing seventy times more energy in the kilovolt range than at radio wavelengths. For Cen A, however, the X-ray and radio powers are comparable, while 200 times more energy occurs in the optical region. The quasar 3C 273 has similar emission at X-ray, radio and visible wavelengths, but radiates two orders of magnitude more flux in the infrared. Obviously many more extragalactic sources must be observed before the nature of any predominant type(s) is revealed.

Spectral information on 3C 273 and Cen A is not good enough, unfortunately, to indicate the nature of the X-ray emission. Meanwhile the X-ray mechanism operating in M87 remains in doubt. Earlier evidence suggested a preference²⁴ for synchrotron emission from the central “jet” seen protruding from the galactic nucleus in low exposure optical photographs. As with the diffuse source in the Crab Nebula, this explanation has the attraction of invoking a common mechanism for the observed continuum radiation in the radio, optical and X-ray wavebands. Again like the Crab, however, the synchrotron model involves a serious lifetime problem with the necessary highly relativistic electrons. Two recent developments have suggested an alternative explanation. First, long baseline interferometric measurements showed the presence of

a very small radio component, less than 2×10^{-3} arc s in diameter, within 1 arc s of the nucleus of M87 (ref. 25). This contains only 2 per cent or so of the overall radiation at 2,300 MHz, but the existence of such a compact source represents the correct conditions for the inverse Compton effect to dominate over the synchrotron process as a means for radiating away the inherent electron energy. Thus electrons of total energy γ times their rest mass energy ($m_0 c^2$) would be more likely to interact with the abundant low energy photons in the source, transferring energy to them by a factor γ^2 and hence shifting infrared and optical light into the X-ray band, rather than slowly radiate away their energy within the local magnetic field as radio photons. Such a small source could quite conceivably be variable on a short time scale, and hence the special interest in reports during the last few months from both the US Navy and MIT research groups that Virgo X-1 has decreased in intensity. The former group find the source weaker in the kilovolt range by a factor of ten.

Diffuse X-ray Background Radiation

The trebling of the number of observed extragalactic sources does not ease significantly the problems of understanding the diffuse X-ray background radiation. This has now been observed from 0.25 keV to 100 MeV and recent data²⁶ have brought evidence for a half power change in spectral index between 20 and 200 keV and significant new limits on the degree of isotropy at 7.7–12.5 keV. It is still generally accepted that the observed isotropy requires an extragalactic origin and the power law spectrum, having also the correct index, suggests strongly that the radiation arises from the same kind of electrons that are responsible for the synchrotron emission of extragalactic radio sources. Among the many models proposed, the most likely invoke either the integrated X-ray emission of normal galaxies²⁷, radio galaxies²⁸, quasars or Seyfert galaxies²⁹, or inverse Compton radiation produced by the electrons leaking out from such extragalactic objects and interacting with the universal microwave blackbody radiation in the depths of intergalactic space³⁰. To explain the observed intensity of the background X-radiation it appears necessary to propose an evolutionary model, in which the production of X-radiation by inverse Compton scattering at an earlier epoch was much greater than at present, particularly in relation to the synchrotron production of radio waves. Comparison of the background radio and X-ray fluxes in terms of the early evolution of radio sources has indicated³¹ that the X-rays arise mainly from an early epoch corresponding to redshifts of the order of four or five. Confirmation of a sharp spectral break would, however, create difficulties for any evolutionary model of the background X-radiation³².

Measurements with a solar spectrometer on board the OSO-3 satellite by the group from the University of California at San Diego have shown the 7.7–12.5 keV flux to be isotropic to 5 per cent over a 20° cell size²⁶. This crude limit is already sufficient to rule out an origin in discrete sources occurring at less than 10^4 per square degree, which includes the emission by normal galaxies. Other reported observations of excess background flux at 0.2–0.3 keV (ref. 33) in the 1–3 MeV band³⁴ and from the Milky Way³⁵ are potentially of great interest, but require careful experimental confirmation before too much effort is devoted to their possible interpretations.

Future Prospects

The future of X-ray astronomy looks bright. The first primary cosmic X-ray satellite, SAS-A, was launched in December 1970 (ref. 36) and will bring a factor of a hundred improvement in sensitivity over current rocket experiments, simply as a result of the greatly extended observation time. Many new sources in the 2–20 keV band and a large number of new source identifications may be expected, yielding information on the relation of X-ray sources to known types of galactic and extragalactic objects. The continuous monitoring capability of the satellite

experiment will be particularly useful in studying X-ray variability and searching for short-lived sources of the Cen X-2 type.

The recently announced UK-5 X-ray astronomy satellite³⁷, due for launch in 1973, will considerably extend these observations and in addition to providing an updated sky survey, will search for line emission and polarization with a sensitivity greatly exceeding that possible during a brief rocket flight, and obtain the broad spectrum of specific sources from 0.2 keV to near 1 MeV.

Observations below 1 keV are likely to open up a whole new range of study in the next few years. At these energies both the interstellar and the intergalactic gas should become gradually opaque. Observations of sources in the galactic plane will thus yield direct information on the abundance of elements such as neon, oxygen, nitrogen and carbon to compare with hydrogen gas densities obtained from radio measurements at 21 cm. Low energy spectral studies of the diffuse X-ray background could be particularly exciting because, if this radiation is indeed of cosmological origin, the characteristic absorption effects of elements such as those mentioned should be detectable, providing information on the cumulative contamination of intergalactic space by exploding galaxies and the like during the earlier life of the universe.

For the primary aim of source identification, the proposed European Lunar Occultation Satellite³⁸ offers the prospect of position determinations to a few arc seconds, a precision that should allow objective searches for galactic sources regardless of assumptions as to the type of object involved. For the study of extragalactic sources this precision would show, for example, whether the M87 source was in the optical jet or the galactic nucleus.

In the further future, NASA intends to fly a large grazing incidence X-ray telescope towards the end of the 1970s on the HEAO-C satellite. The proposed 1,000 cm² mirror is expected to have a spatial resolution of 5 arc s and a sensitivity which will be a further two orders of magnitude beyond SAS-A and UK-5. Such a telescope will be operated rather like a ground-based instrument, in that image tubes, crystal spectrometer, X-ray polarimeters, and so on will be alternately moved into the focal plane. When this stage is reached in X-ray astronomy the observing capabilities will be comparable with those available in the visible region and it is difficult to overstate the astrophysical and cosmological significance of the resulting data.

¹ Friedman, H., *Nature*, **220**, 862 (1968).

² Giacconi, R., Gorenstein, P., Gursky, H., Usher, P. O., Waters, J. R., Sandage, A., Osmer, P., and Peach, J. V., *Astrophys. J. Lett.*, **148**, L129 (1967).

³ Mark, H., Price, R., Rodrigues, R., Seward, F. D., and Swift, C. D., *Astrophys. J. Lett.*, **155**, L143 (1969).

⁴ Cocke, W. J., Disney, M. J., and Taylor, D. J., *Nature*, **221**, 525 (1969).

⁵ Fritz, G., Henry, R. C., Meekins, J. F., Chubb, T. A., and Friedman, H., *Science*, **164**, 709 (1969).

⁶ Bradt, H., Rappaport, S., Mayer, W., Nather, R. E., Warner, B., McFarlane, M., and Kristian, J., *Nature*, **222**, 728 (1969).

⁷ Floyd, F. W., Glass, J. S., and Schnopper, H. W., *Nature*, **224**, 50 (1969).

⁸ Gorenstein, P., Kellog, E. M., and Gursky, H., *Astrophys. J.*, **160**, 199 (1970).

⁹ Grader, R. J., Hill, R. W., and Stoering, J. P., *Astrophys. J. Lett.*, **161**, L45 (1970).

¹⁰ Palmieri, T. M., Burginyon, G., Grader, R. J., Hill, R. W., Seward, F. D., and Stoering, F. D., *Astrophys. J.* (in the press).

¹¹ Lewin, W. H. G., Clark, G. W., and Smith, W. B., *Astrophys. J. Lett.*, **152**, L55 (1968).

¹² Hudson, H. S., Peterson, L. E., and Schwartz, D. A., *Astrophys. J. Lett.*, **159**, L51 (1970).

¹³ Buselli, G., Clancy, M. C., Davison, P. J. N., Edwards, P. J., McCracken, K. G., and Thomas, R. M., *Nature*, **219**, 1124 (1968).

¹⁴ Toor, A., Seward, F. D., Cathey, L. R., and Kunkel, W. E., *Astrophys. J.*, **160**, 209 (1970).

¹⁵ Holt, S. S., Boldt, E. A., and Serlemitsos, P. J., *Astrophys. J. Lett.*, **158**, L155 (1969).

¹⁶ Acton, L. W., Catura, R. C., Culhane, J. L., and Fisher, P. C., *Astrophys. J. Lett.*, **161**, L175 (1970).

¹⁷ Neugebauer, G., Oke, J. B., Becklin, E., and Garmire, G., *Astrophys. J.*, **155**, 1 (1969).

- ¹⁸ Rao, U. R., Jayanthi, U. B., and Prakasarao, A. S., *Astrophys. J. Lett.*, **157**, L133 (1969).
- ¹⁹ Hudson, H. S., Pelling, R. M., Peterson, L. E., and Schwartz, D. A., *Bull. Amer. Astron. Soc.*, **2**, 200 (1970).
- ²⁰ Evans, W. D., Belian, R. D., and Connor, J. P., *Astrophys. J. Lett.*, **159**, L57 (1970).
- ²¹ Kitamura, T., Matsuoka, M., Miyamoto, S., Nakagawa, M., Oda, M., Ogawara, Y., and Tokagishi, K., *Nature*, **224**, 784 (1969).
- ²² Bradt, H., Mayer, W., Naranan, S., Rappaport, S., and Spada, G., *Astrophys. J. Lett.*, **150**, L199 (1967).
- ²³ Bowyer, C. S., Lampton, M., Mack, J., and Mendonca, F., *Astrophys. J., Lett.*, **161**, L1 (1970).
- ²⁴ Adams, D. J., Cooke, B. A., Evans, K., and Pounds, K. A., *Nature*, **222**, 757 (1969).
- ²⁵ Cohen, M. H., Moffet, A. T., Shaffer, D., Clark, B. G., Kellermann, K. I., Jauncey, D. L., and Gulkis, S., *Astrophys. J. Lett.*, **158**, L83 (1969).
- ²⁶ Schwartz, D. A., thesis, Univ. California, San Diego (1969).
- ²⁷ Silk, J., *Astrophys. J. Lett.*, **151**, L19 (1968).
- ²⁸ Bergamini, R., Londrillo, P., and Setti, G., *Nuovo Cim.*, **52B**, 495 (1967).
- ²⁹ Longair, M. S., and Sunyaev, R. A., *Astrophys. Lett.*, **4**, 65 (1969).
- ³⁰ Brecher, K., and Morrison, P., *Phys. Rev. Lett.*, **23**, 802 (1969).
- ³¹ Felten, J., and Rees, M. J., *Nature*, **221**, 924 (1969).
- ³² Longair, M. S., *Mon. Not. Roy. Astron. Soc.*, **150**, 155 (1970).
- ³³ Bunner, A. N., Coleman, P. L., Kraushaar, W. L., McCammon, D., Palmieri, T. M., Shilepsky, A., and Ulmer, M., *Nature*, **223**, 1222 (1969).
- ³⁴ Vette, J. I., Gruber, D., Matteson, J. L., and Peterson, L. E., *Astrophys. J. Lett.*, **160**, L161 (1970).
- ³⁵ Cooke, B. A., Griffiths, R. E., and Pounds, K. A., *Nature*, **224**, 134 (1969).
- ³⁶ Townsend, M. R., and Fichtel, C. E., *Spaceflight*, **2**, 63 (1970).
- ³⁷ *Nature*, **228**, 700 (1970).
- ³⁸ Collet, J., Dilworth-Occhialini, C., Pacault, R., Pounds, K. A., Rocchia, R., Roth, E. R., and Sanford, P. W., *Nature*, **228**, 756 (1970).

Origin of Satellite DNA

by

P. M. B. WALKER

MRC Research Group on the Mammalian Genome, Department of Zoology, University of Edinburgh

The mystery of how satellite DNA came to be so widespread in plants and animals could be solved if this DNA conferred an advantage on the chromosome which carried it. This advantage might be an improved ability to stand up to the rigours of meiosis.

It has been apparent for some time that the chemical organization of the genome of higher organisms presents a considerable enigma. A striking feature of the DNA of many animals and plants is that up to 30% of it may have properties which sharply differentiate it from the remainder. These distinctive fractions are the so-called satellite DNAs and in spite of considerable effort their origin and function remain mysterious. The nub of the problem is that no two species have been shown to share the same kind of satellite DNA, although the presence in one species of a few sequences like those in a satellite from a related species is not ruled out. Because these fractions also consist of multiple repetitions of related sequences, their species diversity implies both that they arise frequently in evolution and that whatever function they may have can be undertaken by many, but not necessarily all, different kinds of sequences. Their function also lacks a strict quantitative requirement, for any proportion of DNA up to about 30% may appear as a satellite fraction.

There is no doubt, however, that the presence of satellite DNA confers some selective advantage; otherwise we cannot account for its spread throughout a population as large as that of the house mouse. Furthermore, the phenomenon is not just confined to a few species and may even be universal. In a recent survey of the mammals, Arrighi *et al.*¹ found that forty-eight of the ninety-three species studied had DNA which showed one or more minor components after banding in a caesium chloride density gradient and which therefore could contain satellite DNA. On the other hand, in one species, man, they found no evidence for a satellite, although a more

sophisticated procedure has demonstrated at least two satellite DNA fractions².

The origin and spread through the population of such diverse sequences therefore present considerable problems, and I would like to suggest that the best explanation might be that satellite DNA confers a direct advantage on the chromosome which carries it, because such a chromosome survives the mechanical processes of, primarily, meiosis better than a sister chromosome not so well endowed. The hypothesis is based on the presence of satellite DNA in the heterochromatic regions of chromosomes and on the sequencing of guinea-pig α -satellite by Southern³ in my laboratory. The latter both shows that the basic sequence is simple and not too unlike the crab dAT satellite⁴ and indicates how such a sequence may have been multiplied during its evolution. I have also drawn on earlier work on *Drosophila*, some of it still controversial, which implicates the heterochromatic regions near the centromere in chromosome behaviour.

Schildkraut and Maio⁵ were the first to demonstrate a possible intracellular localization of the satellite sequences, when they found that DNA, sedimenting with a preparation of nucleoli, was considerably enriched in satellite sequences. Smith⁶ confirmed this result by infecting confluent mouse cells with polyoma virus, which induces a later wave of DNA synthesis. Before the bulk of the new DNA is synthesized, both satellite DNA isolated on density gradients and the nucleoli in autoradiograms are preferentially labelled. Yunis and Yasmineh⁷⁻⁹ have shown that in mouse, guinea-pig and calf a condensed chromatin fraction, prepared by differential centrifugation from ultrasonically disrupted nuclei, contains the bulk of the very different satellite sequences in these three species. Several groups have also shown (refs. 10-12 and personal communications) that after the growth of mouse cells has been synchronized by various procedures, not including polyoma infection, the satellite sequences are synthesized late in the S phase of meiosis. Yasmineh and Yunis are therefore probably correct in considering that heterochromatin is often largely composed of these special repetitive DNA sequences, for late replication is considered to be a universal property of this state of the chromatin¹³. Finally, Jones¹⁴ and Pardue and Gall¹⁵, by *in situ* hybridization, have shown that, in the mouse, satellite sequences are predominantly found near the centromeres during metaphase and near the nucleoli

and heterochromatic granules during interphase. Because both the nucleolar organizer region and the regions near the centromeres are the principal sites of heterochromatin¹⁶ it is difficult to escape the conclusion that heterochromatin is, in many organisms, largely composed of repetitive DNA and that many different kinds of sequences can be repeated. On the other hand, it should be noted that Hennig and I¹⁷ found no satellite visible after density gradient centrifugation and only a small fraction of highly reiterated DNA in *Microtus agrestis* which has a very large amount of heterochromatin.

Amplification

It is often assumed that DNA containing some 10^7 – 10^8 repetitions must have been amplified suddenly at some stage, not necessarily early, in its evolution. Southern³ in his study of the guinea-pig α -satellite noted that not all one-step derivatives of the tetramer —CCCT— occur with equal frequency, and that, for example, —TCCT— occurs about ten times more frequently than —CCCC—. He comments that if the original hexamer had been multiplied 10^7 times and then spread through the guinea-pig population, such a pattern might imply selection for special sequences. This in turn might be used as an argument in favour of a function requiring these sequences. On the other hand, the pattern would be consistent with random base substitution if early multiplication of the sequence had happened over a period long enough to allow mutations to accumulate. Thus one individual could have had, by chance, a longer sequence which was the result of five or so doublings of the original hexamer and which included most of the derived sequences corresponding to the present-day pattern. The genome of this particular guinea-pig was then the site of an event, possibly gene multiplication, which ensured both that the pattern of sequences was multiplied to the degree now found and that this individual became the ancestor as far as satellite sequences are concerned of our present population of guinea-pigs.

Where could such a partially multiplied sequence exist? One candidate is the spacer DNA which separates the blocks of the 28S and 16S ribosomal cistrons^{18,19}. This DNA shares some properties with satellite sequences: it is not transcribed and may have an average molecular weight as much as 6.6×10^6 (ref. 20); it seems to vary in length by as much as a factor of 10 even within one species²¹ and, as D. Brown and A. Blackler (personal communication) have recently shown, its sequence is very different even in two species of *Xenopus* which can interbreed in the laboratory. This DNA is, of course, also in the nucleolar organizer region and takes part in *Xenopus*, but perhaps not in mice, in the only gene amplification process yet known in higher organisms^{22–25}. In addition, Gall *et al.*²⁶ have found a large heavy satellite in dytiscid beetles, of which less than 1% appears to comprise all the ribosomal cistrons of this beetle. Because the evolution of satellite DNA is a rare event compared with the amplification of ribosomal cistrons, we are entitled to suppose that an aberrant amplification of spacer DNA could sometimes occur and that this could be translocated, if necessary, into the centric heterochromatin. Alternatively a sequence in pre-existing heterochromatin could be amplified, and here Gibson and Hewitt's evidence²⁷ on grasshopper supernumerary chromosomes is relevant. Supernumerary or B chromosomes are very small and seem to consist almost entirely of a centromere and adjacent heterochromatic regions. Two pairs of grasshopper populations were studied and it was found that one member of each pair had both a small number of supernumerary chromosomes and a satellite DNA. Moreover, both satellite DNAs seem to have a different buoyant density. These results show that sequence amplification is common and perhaps not sequence specific even in one organism. They also indicate that a centromere surrounded by what may be largely a repetitive sequence is able to coexist with more normal chromosomes.

This leads directly to the hypothesis that a large increase in the amount of DNA in the heterochromatin adjacent to the

centromere might confer a selective advantage not on the individual but on the chromosome which carries it. An earlier proposal^{28,29} that satellite DNA took part in "chromosomal housekeeping" assumed that the sequence was important because it provided specific recognition sites for other molecules, which might, for example, determine how chromosomes fold in mitosis. This idea is now less attractive because of the restricted localization of satellite DNA and because satellite base sequences are seen to be so diverse and so frequently evolved that any function needing the recognition of specific sequence seems improbable. For example, the three closely related species, *Drosophila hydei*, *D. neohydei* and *D. pseudo-neohydei*, all have satellites of different buoyant densities and of different magnitudes (ref. 30 and personal communication). Therefore, if the sequence is important, any molecules binding to these sites must have evolved as rapidly as the DNA, which in turn demands a high degree of selection in favour of divergence. Centromeric localization of satellite, however, would be entirely consistent with another housekeeping function suggested in an earlier review²⁹, namely, the pairing of sister chromosomes at meiosis. Again it is not clear why closely related species need such different sequences for the same function.

On the other hand, a case can be made that mere quantity of DNA near the centromere might confer an advantage on any chromosome carrying it. In *Drosophila* centromeres have been defined³¹ as having different "strengths" on the basis of their behaviour in double first anaphase bridges. A "strong" centromere will pull a "weak" centromere attached by the bridge over to its pole. Lindsley and Novitski³² analysed the nature of centromere "strength" with specially constructed chromosomes. They concluded that it was not the centromere itself but the amount and kind of heterochromatin which could alter the firmness of attachment to the spindle proteins, and that this may reduce the chances of non-disjunction and chromosome loss. There are also examples of an even more direct selective advantage. In maize there is an abnormal 10 chromosome which carries a knob, which at meiosis acts as a neocentromere providing an additional attachment point for spindle proteins³³. In heterozygotes for this chromosome 70% of the female gametes carry the abnormal chromosome, and this is likely therefore to have been caused by the stronger attachment to the egg nucleus pole. In *Drosophila* unpaired chromosomes are often lost at meiosis, and Peacocke has shown³⁴ that X chromosomes with large deletions in their heterochromatin fail to pair with the Y. When this occurs, both X and Y move in a highly non-random fashion both to the same pole. On the other hand, attached XY chromosomes³⁵ which have extra heterochromatin in paired regions on either side of the centromere do not behave like univalents and are recovered at a more normal frequency.

Meiotic Drive

Considerations of this kind have led to the concept of "meiotic drive" as an evolutionary force³⁶, although recently³⁷ some at least of the phenomena so described have been shown to be associated with a failure of sperm maturation. B chromosomes, which, as we have discussed, may be largely heterochromatic, are also interesting from this point of view, since in plants they can be preferentially segregated into the egg nucleus³⁸, despite the deleterious effect on the organism of too many of these chromosomes.

S. W. Brown, commenting on the effect of heterochromatin on chromosome behaviour, says¹⁸: "An extensive series of investigations . . . have shown that heterochromatin is involved in this problem, probably both in contributing to chromosome bulk and more directly in influencing chromosome orientation or centromere potency. . . . The effects occur, however, late in the division cycle and may therefore reflect the physical state of the regions adjacent to the centromere rather than influences analogous to typical gene function". It is not unreasonable to suppose therefore that an increase in the

number of sequences in the heterochromatin may improve the survival of chromosomes. This might be by protecting them from the hazards of meiosis, such as non-disjunction, or more directly by some mechanism like that which occurs in maize, which increases their chances of segregating into the egg nucleus rather than into the polar bodies. It may not be an accident that Pardue and Gall¹⁵ have found that it is only the Y chromosome, which cannot be selected in this way, which contains no satellite sequences. It will also be interesting to see whether the long term survival of chromosomes in heterokaryons³⁹ is affected by their relative endowment of satellite sequences near the centromeres.

A hypothesis on the origin of satellite DNA which relies on selection of chromosomes because of the amount of DNA near their centromere has at least two merits. First, at meiosis just one chromosome of a set can be preferred over its sister. In this way a more gradual build-up of sequences, first in one chromosome then in another, can occur, thus eliminating the difficulties²⁹ engendered by the rapid multiplication and simultaneous translocation of satellite sequences into all chromosomes of a set. Second, the rather quantitative "function" of providing a bulk of suitable DNA makes no stringent requirement for specific sequences. This does not mean that the organism or its viruses cannot exploit the presence of so many similar sequences once they are made. Viral involvement might be suggested by Smith's results⁶ with polyoma, which have already been mentioned. Neither does it mean that satellite DNA can be formed by the multiplication of any short DNA sequence.

Sequence Selection

If any sequence could be used, we would expect every organism to have achieved its optimal dose of centric heterochromatin long ago. Instead, they seem to be continually generating multiple copies of new sequences and, we must suppose, losing old ones. The evidence from the guinea-pig α -satellite³ shows that old satellites probably differ from young ones because of the number of base changes which have accumulated in the original sequence. W. D. Sutton has suggested that this might explain the need for multiplying new sequences. Suppose that a necessary requirement for a satellite sequence was that it should not contain normal control sequences, for example, those for the initiation of transcription or for the despiralization which normally occurs in the euchromatin but not heterochromatin at telophase. Alternatively these short repeating sequences could result in a DNA of special function but of an abnormal conformation like that suggested⁴⁰ for poly d(I-C)-poly d(I-C). Random mutation will sooner or later, depending on the initial sequence, begin to introduce such control sequences or to cause the conformation to revert to normal, and, we would suppose, cause the satellite DNA to act less efficiently. There might then be selection in favour of losing the ineffective sequences and multiplying a new sequence. If in the meantime the source of new sequences, suggested earlier to be spacer DNA, had itself undergone base-substitution, the new satellite would be different from the old.

It may well be that sequence repetition in this kind of DNA is simply a device for ensuring uniformity so that the inevitable attrition of its function by random base substitution occurs uniformly throughout the fraction. The final loss of function will then be wholesale rather than piecemeal, leaving the way clear for a new generation of satellite.

This model predicts that satellites with sequences which are very abnormal and very different from that of the postulated control sequences should have a longer evolutionary life and should perhaps therefore have time to increase to a greater proportion of the genome. The repeating dAT sequence which reaches 30% of the genome in certain crab species⁴¹ might be an example of this. Perhaps Przewalskii's horse, which also has 30% of its genome as a light satellite¹, has another extreme sequence.

This hypothesis of the origin and function of satellite DNA

differs from earlier ideas on housekeeping DNA in that it reduces the part played by specific repetitive sequences and emphasizes the role which might be played by the quantity of DNA in the heterochromatic regions near the centromere. In this way sequences such as the crab dAT, the guinea-pig —CCCTAA— and the mouse sequence containing hexamers like —TTTTTC— can all be accommodated. It does not state that all possible sequences will be found in satellites but, to account for the loss of satellites during evolution, proposes that they may be found to exclude certain sequences with normal main-band functions. The hypothesis proposes a slow build-up of satellite sequences, for each individual chromosome can be favoured over its less endowed sister independently of the rest of the set. There is therefore less need of a sudden saltatory replication to make many millions of copies of the original sequence. It draws attention to the effect on what may be termed chromosome mechanics of variations in the size of the heterochromatin near the centromere, as suggested by certain genetic experiments on *Drosophila*. It is also clear that there are more general genetic implications of the hypothesis if, as in maize, a mechanism could be provided whereby whole chromosomes are selected in spite of the deleterious effect of some markers on the rest of the linkage group.

I thank Dr B. C. Clarke, Professor D. Falconer, Dr E. Southern and Dr W. D. Sutton for suggestions and comments.

- ¹ Arrighi, F. E., Mandel, M., Bergendahl, J., and Hsu, T. C., *Biochem. Genet.*, **4**, 367 (1970).
- ² Corneo, G., Ginelli, E., and Polli, E., *J. Mol. Biol.*, **48**, 319 (1970).
- ³ Southern, E. M., *Nature*, **227**, 794 (1970).
- ⁴ Sueoka, N., *J. Mol. Biol.*, **3**, 31 (1961).
- ⁵ Schildkraut, C. L., and Maio, J. J., *Biochim. Biophys. Acta*, **161**, 76 (1968).
- ⁶ Smith, B. J., *J. Mol. Biol.*, **47**, 101 (1970).
- ⁷ Yasminch, W. G., and Yunis, J. J., *Biochem. Biophys. Res. Commun.*, **35**, 779 (1969).
- ⁸ Yasminch, W. G., and Yunis, J. J., *Exp. Cell Res.*, **59**, 69 (1970).
- ⁹ Yunis, J. J., and Yasminch, W. G., *Science*, **168**, 263 (1970).
- ¹⁰ Bostock, C. J., and Prescott, D., *Exp. Cell Res.* (in the press).
- ¹¹ Tobia, A., Schildkraut, C., and Maio, J. J., *J. Mol. Biol.* (in the press).
- ¹² Flamm, W. G., Bernheim, N. J., and Brubacker, P. E., *Exp. Cell Res.* (in the press).
- ¹³ Lima-de-Faria, A., *Handbook of Molecular Cytology* (edit. by Lima-de-Faria, A.), 277 (North-Holland, Amsterdam, 1969).
- ¹⁴ Jones, K. W., *Nature*, **225**, 912 (1970).
- ¹⁵ Pardue, M. L., and Gall, J. G., *Science*, **168**, 1356 (1970).
- ¹⁶ Brown, S. W., *Science*, **151**, 417 (1966).
- ¹⁷ Hennig, W., and Walker, P. M. B., *Nature*, **225**, 915 (1970).
- ¹⁸ Birnstiel, M., Speirs, J., Purdom, I., Jones, K., and Loening, U. E., *Nature*, **219**, 454 (1968).
- ¹⁹ Brown, D. D., and Weber, C. S., *J. Mol. Biol.*, **34**, 681 (1968).
- ²⁰ Birnstiel, M. L., Grunstein, M., Speirs, J., and Hennig, W., *Nature*, **223**, 1285 (1969).
- ²¹ Miller, O. Z., and Beatty, B. R., *Genetics*, **61**, Suppl. 1, 133 (1969).
- ²² Brown, D. D., and Dawid, I. B., *Science*, **160**, 272 (1968).
- ²³ Evans, D., and Birnstiel, M. L., *Biochim. Biophys. Acta*, **166**, 274 (1968).
- ²⁴ Gall, J. G., *Proc. US Nat. Acad. Sci.*, **60**, 553 (1968).
- ²⁵ Lima-de-Faria, A., Birnstiel, M. L., and Jaworska, H., *Genetics*, **61**, Suppl. 1, 145 (1969).
- ²⁶ Gall, J. G., Macgregor, H. C., and Kidston, M. E., *Chromosoma*, **26**, 169 (1969).
- ²⁷ Gibson, I., and Hewitt, G., *Nature*, **225**, 67 (1970).
- ²⁸ Walker, P. M. B., *Nature*, **219**, 228 (1968).
- ²⁹ Walker, P. M. B., Flamm, W. G., and McLaren, A., *Handbook of Molecular Cytology* (edit. by Lima-de-Faria, A.), 53, North-Holland, Amsterdam, 1969).
- ³⁰ Hennig, W., Hennig, I., and Stein, H., *Chromosoma* (in the press).
- ³¹ Novitski, E., *Genetics*, **37**, 270 (1952).
- ³² Lindsley, D. L., and Novitski, E., *Genetics*, **43**, 790 (1958).
- ³³ Rhoades, M. M., in *Heterosis* (Iowa State College Press, 1952).
- ³⁴ Peacocke, W. J., *Genetics*, **51**, 573 (1965).
- ³⁵ Sandler, L., and Braver, G., *Genetics*, **39**, 365 (1954).
- ³⁶ Sandler, L., and Novitski, E., *Amer. Naturalist*, **91**, 105 (1957).
- ³⁷ Policansky, D., and Ellison, J., *Science*, **169**, 888 (1970).
- ³⁸ Battaglia, E., *Caryologia*, **17**, 245 (1964).
- ³⁹ Rao, P. N., and Johnson, R. T., *Nature*, **225**, 159 (1970).
- ⁴⁰ Mitsui, Y., Langridge, R., Shortle, B. E., Cantor, C. R., Grant, R. C., Kodama, M., and Wells, R. D., *Nature*, **228**, 1166 (1970).
- ⁴¹ Smith, M., *J. Mol. Biol.*, **9**, 17 (1964).

Pre-Mesozoic Oceanic Crust in the Eastern Indian Ocean (Wharton Basin)?

by

ROBERT S. DIETZ & JOHN C. HOLDEN

ESSA, Atlantic Oceanographic and Meteorological Laboratories, 901 South Miami Avenue, Miami, Florida 33130

A search for ocean basins underlain by old crust has suggested that the Wharton Basin would be a likely place to investigate.

THERE is now great interest in the search for old Earth's crust, not only for the sake of a better understanding of ocean floor evolution but also because such material would be more highly mineralized and the thick cover of sediments would offer enticing prospects for petroleum. In what follows, by "old crust" we mean merely pre-Mesozoic crust, older than 225 m.y. Even this modest antiquity would, however, antedate the great sequence of events beginning with the breakup and dispersion of Pangaea, which probably commenced in mid-Triassic, 200 m.y. ago¹.

The half spreading rates associated with seafloor spreading (that is, the spreading on each limb of a spreading mid-ocean rift) of 1–6 cm per year are suggested by the magnetic anomaly growth lines reaching back over the past 4 m.y. If these rates can be extrapolated linearly back in time to anomaly 32 of Heirtzler *et al.*², about half of the ocean floor is of Cainozoic age (less than 65 m.y.)³ except in special situations; nearly all the remainder must be Mesozoic.

The scientific staff on JOIDES (Deep Sea Drilling Project) leg 6 concluded that the North-west Pacific basin was the oldest part of the oldest ocean⁴. Upper Jurassic sediments (Tithonian, 140 m.y.) were encountered in two cores but, by inference, Lower Jurassic or even Triassic ocean floor might be present closer to the Marianas subduction zone. The Philippine Sea, which lies behind the Japan–Marianas–Palau trench system, was found to be young, probably not older than early Cainozoic. (In deep sea drilling, the assumption is made that the age of the sediments immediately overlying basement basalts, as indicated by seismic reflexion profiling, is the age of the oceanic crust. This interpretation is reasonable if the crust was emplaced according to the seafloor spreading concept.)

The search for Palaeozoic crust was also a primary aim of the recent JOIDES leg 11 off the eastern United States⁵. Only mid-Jurassic (about 160 m.y.) strata were found, but this is the oldest rock so far recovered from any ocean basin. This makes it unlikely that the Atlantic commenced opening at the beginning of the Permian and that the peripheral quiet magnetic zone of the Central North Atlantic represents crust emplaced in the 50 m.y. long Kiaman interval of constantly reversed magnetic polarity essentially during the Permian^{6,7}. We agree with Vogt *et al.*⁸ that the magnetic quiet zone represents crustal emplacement during the Triassic. The South Atlantic is clearly younger than the North Atlantic, and so this entire rift ocean (excluding subplates) is unlikely to contain Palaeozoic ocean crust.

It is possible, but perhaps unlikely, that the Arctic Ocean contains old crust. Apparently there was an ancestral Arctic basin within the framework of Pangaea, which we have named *Sinus Borealis* (Latin for northern embayment)⁹. The Eurasian Basin, between the Lomonosov Ridge and Eurasia, must be neo-oceanic, for it contains a central spreading rift, an extension of the mid-Atlantic ridge¹⁰. Perhaps the Canadian Basin

contains old crust. But a likely history for the Arctic Ocean is that the Alpha Ridge in the Canadian Basin is a "fossil" but now abandoned spreading rift. This old rift then "jumped" to its present location, splitting off a sector of the Eurasian craton (the Lomonosov Ridge) in the process¹¹. This would infer that the oceanic crust of the Canadian Basin is not very old, at least in its northern portion. On the other hand, Churkin's¹² interpretation, based on the marginal lower Palaeozoic geosynclines of Alaska and Canada, may be correct. He believes that the oceanic crust of the Canadian Basin must be early Palaeozoic or even Pre-Cambrian.

Seafloor marginal to Antarctica also seems at first to contain sectors of Palaeozoic crust for the following reasons. This continent is surrounded by a rift-megashear system (the pan-Antarctic rift) bounding the Antarctic crustal plate. No trenches are associated with this plate, into which ocean crust is being subducted. It is unique in this respect, for the other major crustal plates—North American, South American, Eurasian, African, Indian, Australian, main Pacific and East Pacific plates—include a subduction zone. Clearly the Antarctic crustal plate has evolved by the outward migration of the pan-Antarctic rift with time. Inside those sectors, where the rift did not initially block out Antarctica's continental slope, areas of old seafloor might be stranded and preserved. The broad sector of West Antarctica which faces the Pacific Ocean seems to offer such a possibility, for this is obviously not a rift margin. A Mesozoic foldbelt, however, a portion of the circum-Pacific orogenic girdle, makes up the periphery of West Antarctica, suggesting that seafloor was once subducted along this margin even if not now. Although volcanic zone extends along the Pacific margin of East Antarctica, the volcanoes are alkaline, not calc-alkaline, and provide no evidence for crustal subduction today. Future seismic profiling, however, will probably indicate the former presence of a trench zone there.

Pursuing the question of old crust, attention is drawn to the so-called subplates. The small ocean basins, such as the Sea of Japan, seem to be of prime interest, for they lie isolated and "protected" behind the subduction zones (trenches) where a descending lithospheric plate is being consumed. Geological and heat flow studies, however, suggest that the Japan Sea is also neo-oceanic¹³. There are Asiatic strata along the inner margin of the Honshu arc, suggesting that Japan was once attached to Asia, but that the Japanese arc subsequently moved outward. Apparently a mid-ocean rift is not a necessity for the emplacement of new oceanic crust, for there are no linear magnetic anomalies in the Japan Sea. The Fuji Basin, behind the Tonga–Kermadec trench, also has been inferred to have young crust¹⁴. It seems likely that the small ocean basins of the Pacific which form subplates are generally neo-oceanic.

The Caribbean is another type of isolated subplate which is protected by a subduction zone—the east by the Antilles trench and the west by the Central American trench. The crust, however, is probably Mesozoic, not Palaeozoic. It was probably created with extension associated with the initial breakup of Pangaea into North America/Eurasia and South America/Africa in the mid-Triassic¹. There is only a small chance that old Pacific floor is trapped within the Caribbean region.

The history of the Gulf of Mexico is an open question

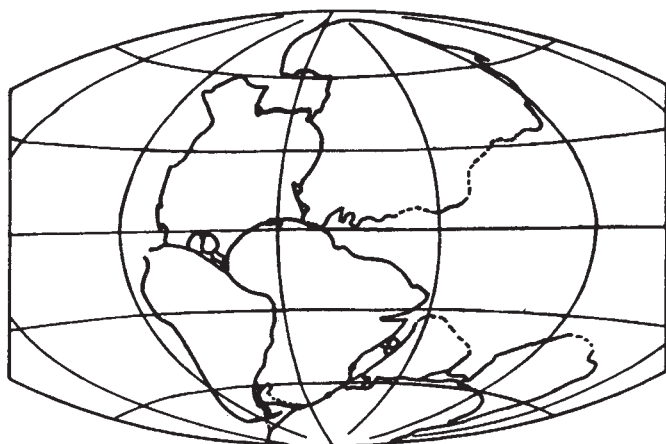


Fig. 1 Reconstruction of the continents into Pangaea before 200 m.y. ago (adapted from Dietz and Holden¹).

depending largely on whether it was an arm of the world ocean (Panthalassa), a *sinus occidentalis*, or was created, like the Caribbean, with the initial breakup of Pangaea. Results from JOIDES leg 10 indicate that the central Gulf of Mexico was already deep water in the late Cretaceous (Santonian, -80 m.y.) and the south-east part since Cainomanian time (-100 m.y.)¹⁵. If the Luann salt is a deep water salt laid down with the initial formation of the Gulf of Mexico, its age would be late Triassic or early Jurassic. It seems most likely that the Gulf of Mexico is neo-oceanic, forming in mid-Triassic with the clockwise rotation of the Honduras and Yucatan blocks which rotated outward to form Central America.

Generally regarded as a rift ocean like the Atlantic, the Indian Ocean would seem at first thought to offer little prospect of containing old ocean floor, but its history is much more

complex than the Atlantic. It differs markedly from the Atlantic Ocean in that there was an ancestral Indian Ocean—namely, the eastern reaches of Tethys. As well as being a rift ocean, it is of the Pacific type, its northern boundary being margined by a subduction zone—the Himalayan–Java trench system. We suggest that the eastern Indian Ocean floor, or the Wharton Basin in the broad sense (as defined by the Ninetyeast ridge, the Java trench, the western Australian margin, and the Diamantina fracture zone), is underlain by pre-Mesozoic crust, for the following reasons.

A generalized reconstruction of Pangaea, adapted from an earlier publication of ours (Fig. 1), shows that the Tethys Sea occupied the region of the Indian Ocean. The region between India and Australia is occupied by a bay of Tethys which we have termed Sinus Australis. A more detailed and precise reconstruction of the continents around Antarctica is shown in Fig. 2, which is quite similar to the assembly offered by Smith and Hallam¹⁶. We believe that this reconstruction is essentially correct and provides a basis on which the subsequent history of breakup and continental drift dispersion in terms of plate tectonics can be reasonably determined and schematized (Fig. 3).

Fig. 3A (a Hammer transverse elliptical projection centred on 90° E longitude and 70° S latitude) shows the probable assembly of the continents around the Indian Ocean before continental drift breakup. Regions to the east of Australia and to the west of India are not considered. India and Australia are joined to Antarctica within the framework of the universal continent of Pangaea before the mid-Triassic, or -200 m.y. In Fig. 3A Antarctica is fixed in position and the geographical coordinates are drawn relative to modern coordinates. This is not entirely gratuitous, for Antarctica probably has remained almost fixed with the other continents doing most of the drifting¹¹.

Fig. 3B shows the situation in the early Cainozoic or about -45 m.y., just before the detachment of Australia from

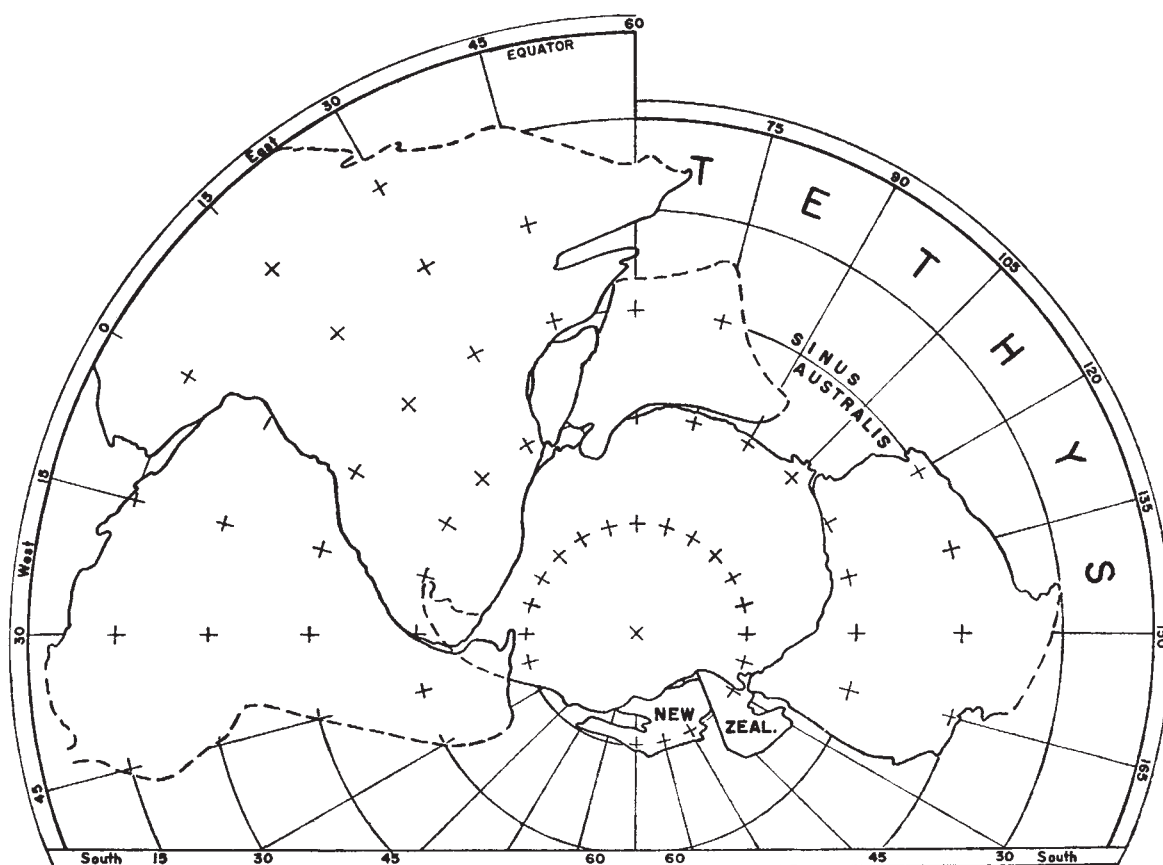


Fig. 2 Detailed depiction showing the reconstruction of continents around Antarctica before 200 m.y. ago. New Zealand has been broken into two parts along the Alpine fault.

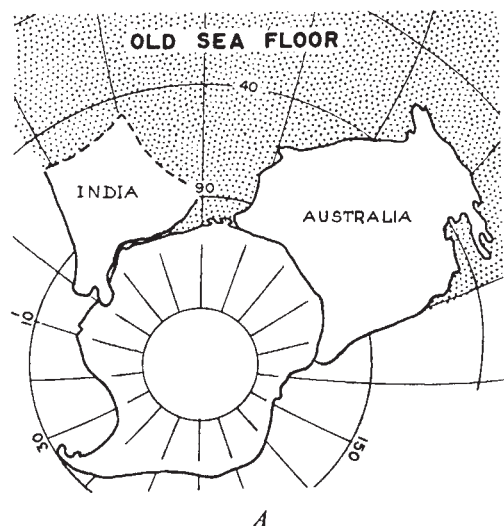
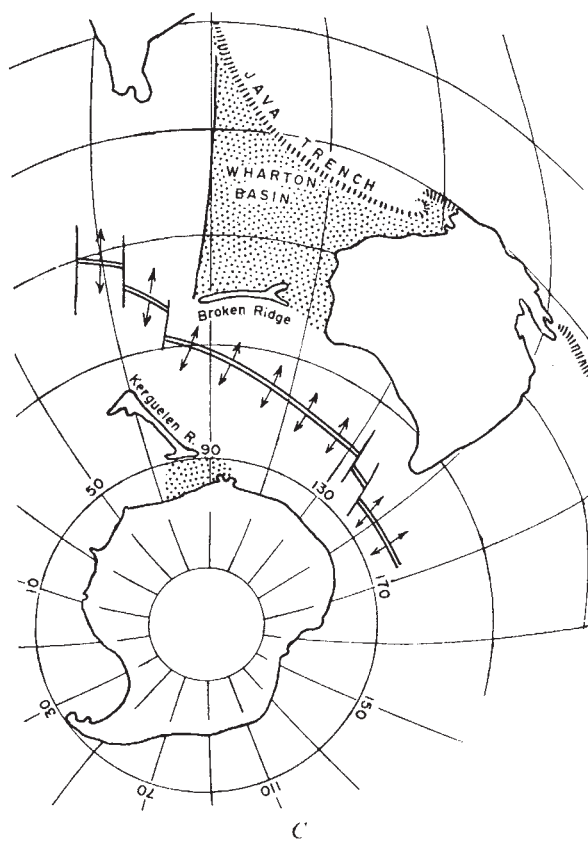
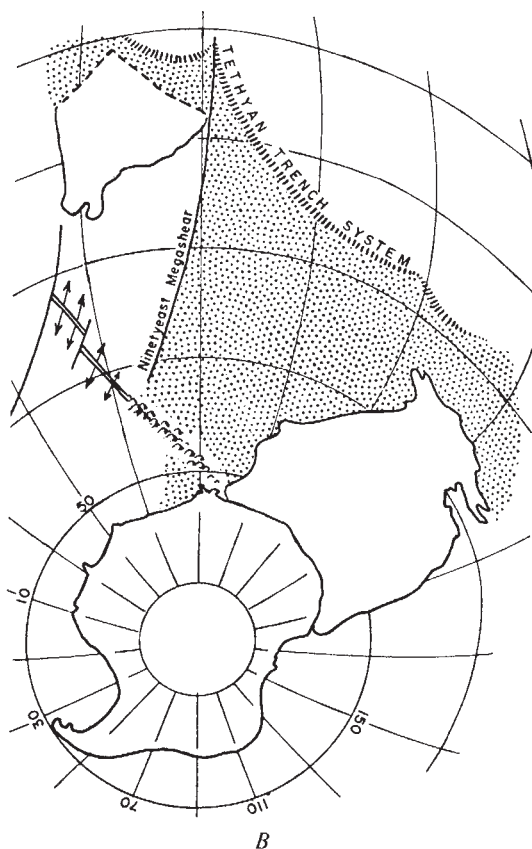


Fig. 3 Time sequence diagram showing the breakup and drift dispersion of India and Australia from Antarctica and consequent preservation of old crust in the Wharton Basin.



Antarctica. India had previously been detached from Antarctica, drifted far northward and almost reached the Tethyan subduction zone (Himalaya "trench"). The Indian plate was bounded on the west by the Chagos-Laccodive megashear and on the east by the Ninetyeast megashear (rift-trench strike-slip transform faults) and on the south by a rift. Old ocean floor was subducted into the Tethyan trench while new ocean crust was emplaced by seafloor spreading in the "wake" of India on both limbs of a northward migrating rift ("mid-ocean ridge"). Thus a broad swath of Tethys was "repaved". An undersea plateau (possibly a partially differentiated outpouring of lava of semi-simatic composition) is shown as having come into existence—the ancestral Kerguelen Plateau-Broken Ridge highground. It had been incipiently split into two parts by the penetration of the India rift.

Fig. 3C shows the position of the continents and the disposition of the crustal plates today. According to the magnetic

reversal chronology impressed on the oceanic crust between Australia and Antarctica, these two continents were not detached until the early Cainozoic, for no anomalies older than anomaly 18 (Eocene, -45 m.y.) are present¹⁷. Consequently the old Tethyan seafloor, especially Sinus Australis, forming the western part of the Australian plate remains undisturbed. This plate later underwent subduction into the Java trench, but the Wharton Basin remains as unconsumed old crust while new ocean floor is being emplaced between Antarctica and Australia. Also, as we have depicted the drift dispersion of continents in this region, a small sector of old crust has been trapped along the margin of Antarctica near 90° E longitude. The reality of such details of this interpretation depends, of course, on the exact timing and geometry of the breakup.

This treatment considers that both Broken Ridge and the Kerguelen Plateau are of simatic composition. If either or both of these features should be identified as microcontinents

there is some evidence that Broken Ridge may be so¹⁸—our proposed history would have to be modified. For example, if Kerguelen proves to be young while Broken Ridge is old, it would most likely have been detached from Antarctica by the rift shown in Fig. 3B and little, if any, pre-Mesozoic crust would remain stranded adjacent to Antarctica.

We have not treated that portion of the Australian plate in the Pacific Ocean to the east of Australia. However, if the New Zealand subcontinent (a reasonable term as the area of the New Zealand platform is almost as large as India) was once attached to Australia, as seems probable, spreading has occurred between these two sialic platforms such that most of the ocean floor in between must be new.

(An alternative solution to closing the Indian Ocean by our continental drift reconstruction is to place India's east coast against Australia. Such a reconstruction leaves a large triangular mediterranean sea within Gondwana, margined by western India, Africa/Madagascar and Central East Antarctica. We suggest that this inland small ocean basin, if it existed (and we are inclined to doubt it) be termed *Mare Gondwanis* (Latin for sea of Gondwana). The breakup of this assembly would then involve the insertion of a spreading rift into the centre of this mediterranean and, in turn, would imply that old ocean floor would now be stranded marginal to parts of India, Africa and Antarctica (from 40°–80° E longitude), the exact sectors involved depending on how the spreading rift was initially inserted. We believe, however, that such a breakup and dispersion history for the Indian Ocean continents is unlikely.)

There is some suggestive evidence that the Wharton Basin is at least of modest antiquity, and its unusual topography supports this interpretation. There are numerous large ridges, marginal plateaus, and blocky highs quite unlike ocean floors elsewhere. This is strikingly revealed by the National Geographic Society's 1967 map of the Indian Ocean floor based on the bathymetric studies of B. C. Heezen and M. Tharp. Sixty million year old basalt has been dredged from Ninety-

east ridge, so that this feature is not young¹⁹. Upper Cretaceous (Turonian) ooze has been cored on the Naturaliste plateau²⁰ and Cretaceous ooze has been recovered from the centre of this basin²¹. Our interpretation awaits testing by seismic reflexion profiling, dredging, coring and, we hope, drilling by the Deep Sea Sampling Project. If our view is correct, the Wharton Basin is the only broad expanse of pre-Mesozoic seafloor in the world.

Received October 20, 1970.

- ¹ Dietz, R. S., and Holden, J. C., *J. Geophys. Res.*, **75**, 26, 4939 (1970).
- ² Heirtzler, J., Dickson, G., Herron, E., Pitman, W., and Le Pichon, X., *J. Geophys. Res.*, **73**, 6, 2119 (1968).
- ³ Vine, F. J., *J. Geol. Education*, **18**, 2, 87 (1970).
- ⁴ *Geotimes*, **14**, 8, 13 (1969).
- ⁵ *Geotimes*, **15**, 7, 14 (1970).
- ⁶ Heirtzler, J. R., and Hayes, D. E., *Science*, **157**, 185 (1967).
- ⁷ Emery, K. O., Uchupi, E., Phillips, J., Bowin, C., Bunce, E., and Knott, S., *Amer. Assoc. Petrol. Geol. Bull.*, **54**, 1, 44 (1970).
- ⁸ Vogt, P., Anderson, C., Bracey, D., and Schneider, E., *J. Geophys. Res.*, **75**, 20, 3955 (1970).
- ⁹ Dietz, R. S., and Holden, J. C., *Sci. Amer.*, **223**, 4, 30 (1970).
- ¹⁰ Dement'skaya, R., and Karasik, A., *Tectonophysics*, **8**, 345 (1969).
- ¹¹ Ostenso, N. A., and Wold, K. I., *Intern. Assoc. Geomag. Aeron. Bull.*, **24**, 67 (1967).
- ¹² Churkin, H., *Science*, **165**, 549 (1969).
- ¹³ Fujii, N., *Intern. Symp. Mechanical Properties and Processes in the Mantle*, Flagstaff, abstract (1970).
- ¹⁴ Karig, D., *J. Geophys. Res.*, **75**, 2, 239 (1970).
- ¹⁵ *Geotimes*, **15**, 6, 11 (1970).
- ¹⁶ Smith, A. G., and Hallam, A., *Nature*, **225**, 139 (1970).
- ¹⁷ Le Pichon, X., and Heirtz, J. R., *J. Geophys. Res.*, **72**, 6, 2101 (1968).
- ¹⁸ Francis, T., and Raitt, R., *J. Geophys. Res.*, **72**, 12, 3015 (1967).
- ¹⁹ Bezrukov, P., Krylov, A., and Cernishev, V., *Oceanologia*, **6**, 261 (1966).
- ²⁰ Burkle, L., Saito, T., and Ewing, M., *Deep-Sea Res.*, **14**, 4, 421 (1967).
- ²¹ Saito, T., *Symp. Micropaleontology of Marine Bottom Sediments* (Special Committee on Oceanic Research, 19, 1967).

New Interpretation of Extragalactic Radio Sources

by

M. J. REES

Institute of Theoretical Astronomy, Madingley Road, Cambridge

The hypothesis that the energy involved in extragalactic violent events derives from the rotational energy of a large number of collapsing stars or pulsar-like bodies in galactic nuclei has been investigated. It shows that extended radio sources may be produced and energized by low frequency electromagnetic waves generated in this way.

THE energy associated with violent activity in quasars and active galactic nuclei is widely believed to be gravitational in origin. A contracting object which conserves angular momentum feeds an increasing fraction of its gravitational binding

energy into kinetic energy of rotation. Rotational braking of compact spinning objects can thus extract a large fraction of their gravitational binding energy. For example, the rotational energy of a neutron star may amount to as much as 10% of its rest mass energy, and it has been shown that more than 40% of the rest energy of a collapsing object can in principle be extracted by rotational torques¹.

Of the many possible mechanisms whereby a compact spinning object can lose its angular momentum, few are more attractive than the suggestion²⁻⁴ that the rotational braking results from emission of electromagnetic waves at the rotation frequency. This mechanism has recently received detailed consideration in connexion with the "oblique rotator" model for pulsars⁵, and it appears that collapsing objects may indeed acquire strong enough magnetic fields to make this a highly efficient process, with the power derived from the rotational energy emerging predominantly in the form of low frequency

electromagnetic waves. If the objects typically have stellar masses, their rotation frequency will be $\lesssim 1$ kHz. The low frequency electromagnetic waves are thus not directly observable, but I shall argue that their indirect effects may be very striking because they will accelerate relativistic electrons very efficiently. In particular, this hypothesis suggests a new interpretation for the phenomenon of extragalactic radio sources.

The low frequency waves could be below the plasma frequency ($\sim 10^4 n_e^{1/2}$ Hz) of the galactic gas, and even below that of the intergalactic gas. They cannot therefore propagate freely from galactic nuclei, but will instead evacuate cavities within which there is no thermal plasma (though relativistic particles may be present). I suggest that extended strong radio sources—Cygnus A, for instance—may actually be cavities of this kind. If this interpretation is correct, the low frequency waves would themselves play the role conventionally assigned to a large scale magnetic field: relativistic particles moving in these waves would radiate, at radio frequencies, by a hybrid synchrotron-inverse Compton process. The particles themselves would either have been ejected, together with the waves, from the nucleus, or else would be accelerated at the cavity boundaries where the waves deposit their energy. The characteristic double structure of strong extended sources can be explained if the galactic nucleus contains a gaseous disk and the low frequency waves escape preferentially perpendicular to its plane. Such waves could be further collimated by “self-focusing” effects which cause the cavity to develop into a long tube. Once this type of situation has established itself electromagnetic waves emanating from the nucleus could be channelled along the tube to feed energy continuously into the source components at the ends.

Low Frequency Wave Fields

A key feature in my proposal is the interaction of matter with intense electromagnetic radiation of very low frequency ($\lesssim 1$ kHz). Before outlining the model, it will therefore be useful to discuss some perhaps unfamiliar aspects of the motion of particles in low frequency electromagnetic waves, and the radiation which they emit.

Consider an electromagnetic wave of angular frequency $\sim \omega$. If the associated energy density is ϵ we can define an equivalent magnetic field H_{eq} with the property that $H_{eq}^2/8\pi \simeq \epsilon$. If the gyrofrequency of a particle in a magnetic field of strength H_{eq} is Ω we can define a parameter $f = \Omega/\omega$. This parameter, which is Lorentz-invariant, is much less than unity in most astrophysical situations. In fact, for f to be of order unity, the radiation brightness temperature T must attain a colossally high value such that $kT/m_e c^2 \simeq \lambda/r_e$, where $\lambda = 2\pi c/\omega$ and r_e is the classical electron radius. But for the very low values of ω that concern us here, f may indeed be $\gtrsim 1$ for electrons—in other words, the equivalent gyroradius may be less than one wavelength.

When $f \ll 1$ the general orbit of an electron consists of non-relativistic oscillatory motion, plus a uniform velocity (which may be zero, or may be highly relativistic). The basic new feature arising when $f \gtrsim 1$ is that there is no frame in which the motion is non-relativistic. For illustration, consider an electron released from rest into a unidirectional beam of linearly polarized radiation. It will be accelerated in the direction of the E-vector. If $f \ll 1$ the electric field of the wave reverses when the electron attains a velocity such that $v/c \simeq f$, and the electron subsequently executes non-relativistic linear oscillations in the direction of the electric field. When $f \gtrsim 1$, however, the velocity becomes relativistic before the electric field reverses. The $\mathbf{V} \times \mathbf{B}$ force then becomes important, and accelerates the particle along the direction of wave propagation. (In this particular case, the particle would be accelerated to an energy $\gamma \simeq f^2$, and would travel $\sim f^2$ wavelengths “downstream” before coming to rest again⁶.)

The general motion of a particle exposed to a monochromatic, unidirectional wave with $f \gtrsim 1$ consists of a uniform translation

plus periodic oscillations with $\gamma \simeq f$. Some detailed calculations of these orbits have been made by Gunn and Ostriker and by Noerdlinger (unpublished work). When the low frequency wave is linearly polarized, the oscillatory part of the orbit is a figure-of-eight lying in a plane perpendicular to the H-vector; in a circularly polarized wave, the motion in the “guiding centre frame” is circular, with Lorentz factor f , in a plane perpendicular (in that frame) to the wave propagation direction. The behaviour, described above, of a particle released from rest can be derived from these results by superposing whatever uniform velocity is required to bring the particle to rest at one point of its cycle.

These exact results refer only to a unidirectional beam at a single well defined frequency. The result that $\gamma \simeq f$ in the guiding centre frame holds, however, in more general circumstances. Particles with $\gamma \gtrsim f^2$ move in wavy lines, the angular excursions about the mean direction of motion being $\sim f/\gamma$. The wavelength would be $\sim 2\pi c/\omega$ if the radiation field were isotropic, but when the radiation is beamed this must be multiplied by $\sim 1 \left(-\frac{v}{c} \cos \theta \right)^{-1}$, where θ is the angle between the

mean velocity and the wave propagation direction. When $\gamma \gg f^2$ particles conserve their energy (except insofar as they lose energy by radiating) even when they travel through a wave field of variable strength.

In the case of a linearly polarized beam, only particles with $\gamma \gtrsim f^2$ can propagate “upstream” with speed c . This is because the Lorentz factor in the guiding centre frame is $\sim f$ so the net velocity of a particle with total energy $\gamma \lesssim f^2$ would be directed “downstream” for part of each cycle. A similar conclusion holds for all cases except that of a purely circularly polarized beam (when the condition is $\gamma \gtrsim f$, not $\gamma \gtrsim f^2$).

The radiation mechanism for particles in electromagnetic waves where $f \gtrsim 1$ is obviously neither standard synchrotron nor inverse Compton emission but is in some sense intermediate between these two processes; I shall refer to it as “synchro-Compton” emission. The emission rate (averaged over an isotropic distribution of particle velocities) is, as usual, proportional to $\gamma^2 \epsilon$. The characteristic frequency is, however, $\sim f \gamma^2 \omega = \gamma^2 \Omega$ and not $\sim \gamma^2 \omega$ as in the standard inverse Compton case. The reason for this close analogy with synchrotron radiation in spite of the very different character of the orbits is that the radiation from a single particle is always beamed in a cone of angle $\sim \gamma^{-1}$, and the particle turns through this angle in a distance $\sim 2\pi c/f\omega$ (that is, in only $\sim f^{-1}$ of a wavelength), consequently feeling a quasi-static field over the relevant period. Another way to understand this result is to transform to the guiding centre frame which moves at a velocity corresponding to a Lorentz factor $\sim \gamma/f$. With respect to this frame the particle performs a relativistic orbit with Lorentz factor f and frequency $\omega(\gamma/f)^{-1}$, and therefore emits synchrotron-type radiation concentrated at frequencies $\sim f^3$ times the orbital frequency. Transforming back from the guiding centre frame boosts the frequency by a further factor $\sim (\gamma/f)$. The approximate spectrum of synchro-Compton radiation from a single particle can also be simply estimated. In the guiding centre frame we expect, by analogy with synchrotron radiation, a spectrum roughly of the form $v^{1/2}$ extending from the peak frequency down to the orbital period, which is a factor $\sim f^3$ lower (though the precise spectrum is obviously a function of the shape of this orbit, which depends on the polarization and directional properties of the low frequency waves). Thus in the rest frame the spectrum should have logarithmic slope $\sim \frac{1}{2}$ from $\sim \gamma^2 \Omega$ down to $\sim f^{-3} \gamma^2 \Omega$. Below the latter frequency, the slope steepens to ~ 1 , as for standard inverse Compton radiation.

The polarization of synchro-Compton radiation from a test particle can be visualized qualitatively by bearing in mind that the only relevant electrons are those moving towards the observer (to within an angle $\sim \gamma^{-1}$), and that the E and $\mathbf{V} \times \mathbf{B}$ contributions to the transverse acceleration are of comparable

importance. As regards linear polarization the results closely resemble those for the standard inverse Compton case. If the low-frequency waves are linearly polarized, the synchro-Compton emission is linearly polarized, to a comparable degree, in the direction of the projected E -vector.

If the low frequency wave is circularly polarized, the synchro-Compton radiation is also circularly polarized to a degree $\sim 0.6 f^{-1}$ (ref. 7). Note that this is independent of the particle's total energy, in contrast to the situation in standard synchrotron theory⁸, where the circular polarization $\propto \gamma^{-1}$, and would be negligible, except perhaps at long radio wavelengths, in most astronomical contexts.

The above results apply to test particles the influence of which on the propagation of the electromagnetic wave can be neglected. The standard propagation condition is that $\omega > \omega_p$, when

$$\omega_p \simeq \left(\frac{4\pi n_e e^2}{n_e} \right)^{\frac{1}{2}}$$

is the formal plasma frequency (numerically, $\omega_p/2\pi \simeq 9 \times 10^3 n_e^{\frac{1}{2}}$ Hz). This criterion must, however, be modified when as is inevitable when $f \gtrsim 1$, the electrons are relativistic. The propagation condition is then the less stringent one that $\omega > \omega_p'$, ω_p' being a modified plasma frequency given by $\omega_p' \simeq \omega_p < \gamma^{-1} >^{\frac{1}{2}}$ (ref. 9).

Even when $\omega > \omega_p'$ the propagation of the wave may be modified because the effective refractive index

$$\mu = 1 - \left(\frac{(\omega_p')^2}{\omega^2} \right)^{\frac{1}{2}}$$

experienced by the low frequency wave differs significantly from unity. This has two important effects. First, the group velocity of a beam of radiation ($\propto \mu$) is reduced, so the energy density ϵ associated with a given flux is proportionately increased (without, however, a corresponding increase in the longitudinal pressure). This affects the intensity of the synchro-Compton emission from each particle. Second, the $\langle E^2 \rangle / \langle B^2 \rangle$ ratio in the wave varies as μ^{-2} . This changes the relative strength of the E and $V \times B$ forces on relativistic electrons, with the interesting consequence that the synchro-Compton radiation of particles in an unpolarized beam displays linear polarization in a plane perpendicular to the propagation direction⁷. The possible degree of polarization is $\sim (1 - \mu^2)/(1 + \mu^2)$ for radiation emitted at right angles to the beam. When $\mu \neq 1$ the shape of the particle orbits in the guiding-centre frame will differ somewhat from the orbits of test particles, and this modifies the detailed synchro-Compton spectrum from each particle.

The detailed interaction of charged particles with strong low frequency electromagnetic waves warrants and requires a great deal of further study. For the purposes of this discussion, however, the essential points are: (i) all electrons exposed to a wave with $f \gtrsim 1$ become relativistic; and (ii) such electrons emit "synchro-Compton" radiation, which has the same characteristic frequency and intensity as synchrotron radiation in a field H_{eq} and which may be polarized.

Outline of Source Model

As a preliminary step towards a radio source model, I shall investigate the effects of introducing a localized source of low frequency electromagnetic waves into a homogeneous hydrogen plasma of electron density n_e . Suppose that the wave source radiates at an angular frequency ω , and that after switching on it maintains a constant luminosity L . The intensity parameter of the waves would then, neglecting attenuation, vary as $f \propto R^{-1}$.

If $\omega > \omega_p$ the wave can propagate indefinitely without being impeded by plasma effects. It nevertheless heats the surrounding plasma by directly accelerating electrons, and also via

free-free absorption, and in consequence suffers some attenuation.

In the more interesting situation where $\omega < \omega_p$ the wave cannot propagate unless it can either accelerate the surrounding electrons to such high γ that the effective plasma frequency $\omega_p'^1 \simeq \omega_p < \gamma^{-1} >^{\frac{1}{2}}$ falls below ω , or else force the matter out ahead of it. When

$$f \gtrsim f^* = \left(\frac{m_p}{m_e} \right)^{\frac{1}{2}} \left(\frac{\omega_p}{\omega} \right)$$

as will obviously be the case sufficiently close to the central object, the wave is not seriously impeded because its pressure is sufficient to impart relativistic outward velocities to all the material it encounters. But when, at later times, the influence of the wave penetrates to a larger radius $R \gtrsim R^*$, for which $f \lesssim f^*$, the radiation no longer has enough momentum to propel all the external matter (both protons and electrons) out of its way at speed $\sim c$. At this stage there are two possibilities. Either (a) the wave can accelerate the electrons to a sufficiently high γ to make $\omega_p' \gtrsim \omega$, so that it can continue to propagate outward at $\sim c$ without dragging the matter with it, or (b) the wave does not penetrate beyond a fairly well-defined boundary at a distance R from the centre, where it is absorbed (the energy going mainly into fast particles) or reflected.

Alternative (a) will only occur if

$$f > \left(\frac{\omega_p}{\omega} \right)^{2*}$$

which is not fulfilled unless

$$R < R^* \left(\frac{m_p}{m_e} \right)^{\frac{1}{2}} \left(\frac{\omega_p}{\omega} \right)^{-1}$$

Thus if

$$\left(\frac{\omega_p}{\omega} \right) > \left(\frac{m_p}{m_e} \right)^{\frac{1}{2}}$$

this never happens when $R > R^*$, and in any case it is always violated at sufficiently large distances from the central wave source. This generation of electromagnetic waves at frequency ω in a medium for which $\omega_p > \omega$ inevitably leads to a situation resembling alternative (b), where the wave energy is deposited within an expanding cavity.

When $R \gg R^*$ the expansion rate $\dot{R}$ of the cavity is governed by a balance between the internal pressure and the "ram pressure" $n_e m_p \dot{R}^2$ of the external matter, and we then have $\dot{R} \ll c$. Even though all the momentum of the electromagnetic waves is transferred to the matter at the cavity boundary, only a fraction $\sim \dot{R}/c$ of the wave energy goes into bulk kinetic energy. Thus unless the waves are reflected with high efficiency from the boundary (and some preliminary calculations suggest that this is very unlikely) almost all the wave energy must go into random particle motions. Because of the lower inertia of electrons, much more than half this energy probably accelerates relativistic electrons. If these electrons remain trapped within the cavity—because, for example,

* One might think the relevant criterion should, instead, be the less stringent one that $f > (\omega_p/\omega)$ because, as discussed in the last section, a test electron is accelerated to an energy $\gamma \simeq f^2$. However, the presence of the accompanying protons reduces the efficiency of the acceleration, since the acceleration of electrons in the wave direction is then opposed by electrostatic forces, and no significant charge separation can occur. The average electron then acquires an energy corresponding only to $\gamma \simeq f$.

streaming instabilities or weak magnetic fields inhibit their escape—the expansion obeys

$$\dot{R} \simeq \left(\frac{R}{R^*}\right)^{-3/2} c \text{ (i.e., } R \propto t^{3/5})$$

The cavity would expand somewhat slower if the particles leaked out or radiated their energy away.

Without studying in detail the interaction of the low frequency electromagnetic waves with the cavity boundary, we cannot determine how many electrons are accelerated, nor their energy spectrum. It is curious, if no more, that a calculation of the energy spectrum of the relativistic electrons generated over the whole development of the cavity (including the stage when its radius is $< R^*$), based on the simplest conceivable assumptions, yields a differential number spectrum $N(E) \propto E^{-5/2}$ at energies above $m_e c^2$ (~ 1 BeV), with a “break” at energies below this. This is, of course, strikingly reminiscent of the typical electron spectra in non thermal sources.

On the assumption that most of the wave energy goes into electrons, which are therefore trapped within the cavity, the following simple argument places a lower limit on the mean electron energy. If the available energy were shared between too many particles, then the waves would no longer be free to propagate to the edge of the cavity. The condition that the refractive index within the cavity be real then requires

$$<\gamma^{-1}>^{-1} \gtrsim \left(\frac{\omega_p}{\omega}\right) \left(\frac{m_p}{m_e}\right)^{1/2} \left(\frac{R}{R^*}\right)^{-2/3} \quad (1)$$

This means that, as the cavity develops, the wave energy is absorbed by a progressively smaller fraction of the matter, the remainder being pushed outwards by the ram pressure. (There would be a strong shock wave ahead of the interface where the radiation is absorbed. Behind this shock, the density would be ~ 4 times its ambient value. The condition that the waves are unable to propagate freely should therefore, strictly speaking, be $\omega < 2\omega_p$, not $\omega < \omega_p$.) Also, the wave pressure confines particles of a given γ to the outer parts of the cavity where $f \lesssim \gamma^{1/2}$. Only those particles with very high energy can approach close to the central object.

The relativistic electrons in the cavity, being exposed to the low frequency wave, will emit synchro-Compton radiation at a rate governed by the wave energy density. In convenient units

$$H_{eq} \simeq 3 \times 10^{-4} \left(\frac{L}{10^{46} \text{ erg s}^{-1}}\right) R_{kpc}^{-1} \mu^{-1/2} \left[\frac{\Theta}{4\pi}\right]^{-1/2} \text{ G} \quad (2)$$

In equation (2) we have not allowed for the enhancement of the wave energy density which could result from reflexions at the boundary. Although we have so far assumed that the central source emits isotropically and creates a spherical cavity, the factor $[\Theta/4\pi]^{-1/2}$, where Θ is an effective solid angle, is included for the purposes of our subsequent discussion of collimated wave sources.

I shall now investigate whether it is quantitatively plausible to explain the emission from extended radio sources in terms of synchro-Compton radiation from cavities of this kind. The most obvious feature of observed strong sources is that they are not spherically symmetric, but characteristically comprise two components, one on either side of the parent object. We must plainly, therefore, invoke a collimated, rather than isotropic, output of low frequency waves. For the moment we merely postulate the appropriate degree of collimation, estimating it from the observed ratio of component size to separation. But I shall show below that this is by no means an *ad hoc* hypothesis—there are several mechanisms which tend naturally to concentrate wave energy from galactic nuclei into narrow directed beams.

When the waves from the central source are beamed, the

cavity that they create will be cone-shaped rather than spherical, but my discussion still applies, provided only that the appropriate Θ is included in equation (2).

Consider, as an illustration, the archetype extended double source Cygnus A, for which a detailed 5 GHz map is available¹⁰. The ratio of component diameter to separation is about 1 : 13. The effective solid angle of the beam, allowing for both components, would then have to be ~ 0.01 ster. The components are ~ 50 kpc distant from the central galaxy. From equation (2) we then find an equivalent magnetic field of $H_{eq} \simeq 2 \times 10^{-4} \mu^{-1/2} \text{ G}$ for $L \simeq 10^{46} \text{ erg s}^{-1}$. This is comparable with the equipartition field $H_1 \simeq 3 \times 10^{-4} \text{ G}$ estimated on the assumption that most of the relativistic particles are electrons. (Note also that μ may be depressed significantly below unity and H_{eq} correspondingly raised by the relativistic plasma within the components.) Therefore a suitably collimated wave, corresponding to an energy output $10^{46} \text{ erg s}^{-1}$, could play the role of a magnetic field in the components of Cygnus A. For these parameters,

$$f \simeq 1,000 \left(\frac{\omega}{2\pi}\right)^{-1}$$

and so if the characteristic frequency were, say, ~ 10 Hz the waves would (from equation (1)) be capable of accelerating electrons to the required BeV energies in the components, and could prevent them from diffusing inwards towards the central galaxy. The source energetics estimated by Mitton and Ryle¹⁰ still apply. The energy content of each component would be $\sim 10^{58} \text{ erg}$. If the components are confined by the ram pressure of external matter, the density of the latter must be $n_e \simeq 10^{-4} \text{ cm}^{-3}$ (which corresponds to $\omega_p \simeq 100 \text{ Hz}$ and is certainly high enough to prevent ~ 10 Hz waves from propagating freely). The energy expended in driving the components outward through this medium would be $\sim 10^{60} \text{ erg}$. In conventional theory, this must come from the kinetic energy of thermal gas contained within the radio components. In our picture, however, the density of matter must be even lower within the components than outside, and the inertia negligible. The required 10^{60} erg is instead provided by the continuous thrust of electromagnetic waves emerging from the galactic nucleus. The fact that this greatly exceeds the energy currently present in the components guarantees that the wave pressure can control the dynamics of the relativistic particles, and also implies that efficient particle containment is unnecessary. (It is a general property of “ram pressure confinement” models that the total energy requirements exceed the current energy content by a factor $\sim \Theta^{-1/2}$.)

Cygnus A is, of course, an exceptionally powerful source. In more typical cases, the infrared luminosity (in the form of low frequency waves) of the associated galactic nuclei is of order $10^{44} \text{ erg s}^{-1}$.

What processes might cause the collimation of the low frequency waves indicated by the observed size/separation ratio of double sources? The initial bifurcation, and a certain degree of beaming, could arise in the galactic nucleus itself in the following way. The objects (whatever they may be) that generate the waves are probably embedded in a gravitationally bound gas cloud, of density $\sim 10^6 \text{ particles cm}^{-3}$, which is responsible for the optical emission lines characteristic of active galactic nuclei. We then would have a situation similar to the classic two-fluid Rayleigh-Taylor instability, where the radiation, playing the role of the lighter fluid, is produced at a lower gravitational potential than most of the gas. Gravitation is significant only in the compact nucleus itself, and has a negligible effect on the growth of the cavity. Although the cavity boundary is decelerating (thus mimicking the effect of a gravitational force) this situation is not Rayleigh-Taylor unstable, because the denser medium is on the outside. The radiation will then escape by blowing out a bubble or jet in a particular direction. Even if the angular momentum per unit mass were comparatively small, the compact gas cloud

would be flattened into a disk. The waves and relativistic particles generated within the disk would then obviously tend to break out preferentially in the direction of the axis. Thus, even a few parsecs from the nucleus, the waves will form two beams aimed in opposite directions.

Though this process would probably not in itself provide a sufficiently narrow and well-directed beam to explain the average double source, it may initiate an interesting "self-focusing" mechanism which collimates the waves more precisely as they propagate further from the nucleus (inflating a cavity as they go). We can visualize this mechanism as follows. Suppose that the waves emerge from the nucleus with a conical beam pattern, the intensity $L(\Phi)$ being greatest on the cone axis ($\Phi=0$) and being a decreasing function of Φ . The waves will create a conical cavity. The evacuation would be more complete, and any remaining particles more energetic, along the axis than towards the edges of the cone. Consequently, the refractive index $\mu(\omega)$ at a particular distance from the nucleus would decrease with increasing Φ . So, as the waves progress outwards, they will tend to converge towards the cone axis. The angular spread therefore reduces, and the effective solid angle (θ) decreases as the cavity grows. This can lead to a "wave guide" situation, in which the cavity has the form of a tube, along which waves are channelled, through repeated reflexions at glancing incidence from the sides, to the components at the ends. (Reflexions at glancing incidence, unlike those at normal incidence, need not entail significant absorption.) This type of situation could provide enough collimation to explain Cygnus A, and even more extreme examples, provided that the asymmetry of the nucleus produced enough directivity to initiate the focusing mechanism. Note that the "wave guide" need not be straight—indeed, if it is expanding into a medium of non-uniform density, it will tend to curve towards regions of lower density.

Value of the Hypothesis

The hypothesis that extended radio sources are produced and energized by low frequency electromagnetic waves generated in the nucleus of the parent object seems at least a promising one. My treatment has plainly oversimplified an exceedingly complicated phenomenon, but has indicated that the pressure of the low frequency waves can inflate a cavity (which, if the waves are suitably collimated, could mimic the shapes of observed sources), and that the wave energy can be transformed with high efficiency into relativistic electrons. The observed radio emission would be synchro-Compton radiation from these electrons. The large scale ordered magnetic field, the origin of which poses a severe problem for all theories involving the ejection of plasma clouds from the galactic nucleus, then becomes quite redundant. Also, the well known problems associated with adiabatic losses are evaded, because power generated in the centre can naturally be channelled along the evacuated cavity (coinciding with the axis of the source) to feed energy continuously into the components at the ends. If a "wave guide" type of situation can be established, the longitudinal wave pressure will continually push the components radially outward against the ram pressure of intergalactic matter, and it seems possible to account for those double sources (for example 3C 33) in which the components are even smaller compared to their separation than those of Cygnus A.

The brightness distribution over the components depends on the distribution of relativistic electrons and wave intensity in the "head" of the cavity, and cannot be predicted without detailed calculations of the inhomogeneous relativistic plasma involved. The general shape of the components, however, may still be determined principally by the considerations of De Young and Axford¹¹. Transverse confinement would be more easily achieved in my model because (except at the ends) the cavity would contain only outward-directed waves and particles which contribute little transverse pressure. It is,

likewise, hard to predict the form of the radiation spectrum. Naive arguments suggest that particles accelerated at the cavity boundary must attain energies satisfying equation (1), but almost certainly complex wave-particle interactions will be operative, and these may even be able to establish the "standard" power law electron spectrum with slope -2.7 (ref. 12). Also, many of the electrons, at least those with higher energies, may have been accelerated in the galactic nucleus and then ejected.

The polarization properties of the synchro-Compton radio emission from the source components depend on the polarization of the low frequency wave field, and on the refractive index of the medium through which the waves are propagating. If the nucleus contained a large number of independent spinning objects with rotation axes which were randomly oriented, then the low frequency waves would be unpolarized. Thus if $\mu \approx 1$ in the cavity, the synchro-Compton radiation would be unpolarized also, but if the refractive index (at the frequency ω) were depressed significantly below unity, the observed radiation would tend to be linearly polarized perpendicular to the source axis. The situation may, however, be confused by refraction of the low frequency waves, and also by possible anisotropies in the electron velocity distribution.

If the spinning objects were all oriented the same way—as might be expected if, for example, they resulted from fragmentation of a supermassive object or a spinning disk—the source might display different linear polarization properties, and conceivably circular polarization as well, because the low frequency waves could then be elliptically polarized.

My discussion of extended radio source components depends on the assumed characteristic frequency ω of the low frequency waves, and on the power L emerging from a galactic nucleus in this form, but is otherwise independent of the precise origin of the waves. Indeed, I have placed no further constraints on the nature of the central nucleus, apart from requiring that it must somehow (perhaps in the fashion suggested earlier) provide the initial bifurcation and collimation needed to account for the characteristic double structure of strong extended sources.

The entities that generate the waves may be individual collapsing stars which, because of their high magnetic fields and small deviations from axisymmetry, radiate their rotational energy electromagnetically rather than through gravitational radiation. Bardeen¹ has shown how up to 42% of the rest energy of a spinning body could be radiated in this way. Alternatively—and this is perhaps the most "conservative" assumption at present—we may (following Burbidge's¹³ model for M87) envisage large numbers of pulsar-like bodies, perhaps formed as remnants of supernovae, which radiate in the manner postulated by the "oblique rotator" model. (As a third possibility, it is conceivable that a differentially rotating disk of the kind Lynden-Bell¹⁴ has considered could develop flares which generate low frequency waves.) All that is necessary is that the characteristic wave frequency should be somewhere in the range 1–1,000 Hz, which is typical of the rotation or pulsation frequency for stellar-mass objects of dimensions comparable with their Schwarzschild radii. The required conditions would certainly be expected to occur according to the stellar collision model for violent events, but could also result from fragmentation of a single supermassive object. A firmer estimate of the masses of the individual emitting objects is important insofar as the characteristic frequency, ω , depends on it. We have seen how the value of ω determines the energies to which typical electrons are accelerated, and also controls the extent to which they are concentrated towards the boundaries of the cavity.

(The idea that galactic nuclei contain single supermassive rotating objects has returned into vogue because of the alleged periodic behaviour of the QSS 3C 446. It is hard to see how such an object, rotating rigidly, could remain invulnerable to general relativistic instabilities until it had contracted enough to yield up a substantial part of its rest mass energy in useful

form. Even so, the characteristic rotation period of such an object would be days or months. An exceedingly small charge density suffices to carry the currents associated with oscillations of such long period. Thus a "spinar" would emit magnetohydrodynamic waves frozen into the plasma, rather than electromagnetic waves (in which the displacement current is important). My considerations are thus not relevant to this situation. Piddington¹⁵ has discussed a possible connexion between "spinars" and extended radio sources.)

It is interesting to speculate on possible more direct manifestations of hypothetical discrete spinning objects, of stellar mass, in galactic nuclei. The formation of each may be associated with a supernova-type event, and the bulk of the rotational energy may emerge in a burst lasting $\lesssim 1$ yr. (According to the "oblique rotator" model, the Crab pulsar would have an initial slowing down time scale of ~ 1 yr if it formed with nearly the break-up angular velocity.) Each newly formed object, emitting intense electromagnetic waves at its rotation frequency, would blow out a cloud of relativistic particles, probably at speed $\sim c$. It is tempting to identify these exploding clouds with the variable components observed at high radio frequencies from compact sources¹⁶. The integrated radio output from each outburst is typically 10^{52} – 10^{53} erg which is comfortably less than the available gravitational energy from an object of a few solar masses. Successive outbursts typically recur at intervals of 1–2 yr in the strongest sources. This corresponds to an average power $\sim 10^{46}$ erg s^{-1} , comparable with the case of Cygnus A.

A more speculative possibility, suggested by analogy with the observed properties of pulsars, is that these spinning objects may radiate intense coherent pulses in the radio band, principally at frequencies $\lesssim 100$ MHz. If this were so, there would be compact low frequency radio sources in some galactic nuclei. In this connexion the evidence for a component in 3C 273 B with a spectrum which rises steeply towards low radio frequencies in a manner reminiscent of pulsar spectra is especially suggestive (C. Hazard, private communication). Because the emission would probably be dominated by the few most recently formed (and therefore most rapidly spinning) objects, substantial variability might be expected. These objects may be responsible for some of the optical continuum as well, so that it would not necessarily prove fruitless to search for optical fluctuations on even shorter time scales than those already detected. Such observations would seem intrinsically worthwhile, irrespective of the credibility of the present theoretical model.

In many cases, of course, absorption by the surrounding gaseous disk would preclude observation of any radio emission emanating directly from the nuclear regions. (Also, quite apart from the possibility of absorption, the absence of evident activity in the nucleus would not argue strongly against the view that the nucleus provides a continuous power supply into an extended source surrounding it. As an analogy, the Crab Nebula is believed to derive all its energy, in some manner, from the pulsar NP 0531, whereas the directly observable emission from the latter is small compared with that from the whole nebula.)

The detailed development of an extended source through the period of activity of the parent galaxy will obviously depend on the power output L from the nucleus, and on ω . A fuller treatment should consider a spectrum for the low frequency waves, instead of characterizing them by a single frequency. For a given L , the cavity expands at a rate dependent on the degree of collimation and the external density. This density will not be a constant, but is likely to decrease by a large factor as the cavity penetrates from the galaxy to

the halo and then to the intergalactic medium. There should also be significant differences between sources associated with galaxies in clusters and those associated with field galaxies. (Interesting instabilities may occur if the external gas is only partially ionized.) The value of L determines the rate of production of relativistic particles, the speed at which the cavity inflates, and H_{eq} . Furthermore, L may be time-dependent. Complex sources with more than two components—Centaurus A or 3C 129, for example—are conventionally interpreted in terms of successive ejections of "plasmoids" (though this view has the consequence that later outbursts are always inferred to have been less violent than the first, which seems somewhat unpalatable). In my model the inner components could merely be regions of enhanced particle density within the cavity. In such regions the radio emission per electron would be increased, because the higher particle density would reduce μ , and so raise ϵ .

Another complex system for which a new interpretation suggests itself is that associated with NGC 1275 (3C 84). Radio emission from two neighbouring galaxies, NGC 1265 and IC 310, seems in some way to have been triggered by 3C 84. Ryle and Windram¹⁷ suggest that the radio emission from the two neighbouring galaxies may be due to relativistic electrons ejected from 3C 84. It is also conceivable, however, that 3C 84 emits electromagnetic waves which are just able to propagate through the intervening medium but which are absorbed (and generate relativistic electrons) when they impinge on NGC 1265 and IC 310. It is not unlikely that all types of extragalactic radio source, including such peculiarities as the jets in 3C 273 and M87, can be accommodated in this general scheme.

If the output of wave energy from the nucleus suddenly lapsed, the radio emission would fade on a time scale comparable with the light travel time across the source (unless reflexions of the waves at the boundaries were very important). Van der Laan and Perola¹⁸ argue that a sudden fading of this kind, which would be hard to understand in other theories, is implied by the spectral data on 3C sources. Because of this, and also because confinement of particles within the radio cavity is unlikely to be efficient, the model indicates that there may be a large reservoir of relativistic electrons in intergalactic space (which would be relevant to, for example, theories of the X-ray background).

In conclusion, the hypothesis that the bulk of the power from active galactic nuclei emerges as very low frequency electromagnetic waves seems to lead—without further assumptions—to an attractive interpretation of the chief puzzling features of extragalactic radio sources.

Received December 15, 1970.

- ¹ Bardeen, J. M., *Nature*, **226**, 64 (1970).
- ² Hoyle, F., Narlikar, J. V., and Wheeler, J. A., *Nature*, **203**, 914 (1964).
- ³ Wheeler, J. A., *Ann. Rev. Astron. Astrophys.*, **4**, 393 (1966).
- ⁴ Pacini, F., *Nature*, **216**, 567 (1967).
- ⁵ Ostriker, J. P., and Gunn, J. E., *Astrophys. J.*, **157**, 1395 (1969).
- ⁶ Jory, H. R., and Trivelpiece, A. W., *J. Appl. Phys.*, **39**, 3053 (1968).
- ⁷ Rees, M. J., *Intern. Astron. Union Symp.* No. 46 (edit. by Davies, R. D., and Smith, F. G.) (Reidel, in the press).
- ⁸ Legg, M. P. C., and Westfold, K. C., *Astrophys. J.*, **154**, 499 (1968).
- ⁹ Zhelezakov, V. V., *Soviet Astron.*, **11**, 33 (1967).
- ¹⁰ Mitton, S. A., and Ryle, M., *Mon. Not. Roy. Astr. Soc.*, **146**, 221 (1969).
- ¹¹ De Young, D. S., and Axford, W. I., *Nature*, **216**, 129 (1967).
- ¹² Tsytovich, V. N., and Chikhachev, A. S., *Soviet Astron.*, **13**, 285 (1969); and **14**, 385 (1970).
- ¹³ Burbidge, G. R., *Astrophys. J.*, **159**, L. 105 (1970).
- ¹⁴ Lynden-Bell, D., *Nature*, **223**, 690 (1969).
- ¹⁵ Piddington, J. H., *Mon. Not. Roy. Astron. Soc.*, **148**, 131 (1970).
- ¹⁶ Kellermann, K. I., and Pauliny-Toth, I. I. K., *Ann. Rev. Astron. Astrophys.*, **6**, 417 (1968).
- ¹⁷ Ryle, M., and Windram, M. D., *Mon. Not. Roy. Astron. Soc.*, **138**, 1 (1968).
- ¹⁸ Van der Laan, H., and Perola, G. C., *Astron. Astrophys.*, **3**, 408 (1969).

* It is true that some estimates of the energies involved in these outbursts yield values much higher than this. These estimates, however, are based on the assumption of an adiabatically expanding magnetic field, and are altered if we attribute the observed radio flux to synchro-Compton emission in the electromagnetic waves continually generated by the spinning central remnant of the explosion.

RNA Dependent DNA Polymerase Activity in Mammalian Cells

by

EDWARD M. SCOLNICK, STUART A. AARONSON,
GEORGE J. TODARO & WADE P. PARKS

Viral Lymphoma and Leukemia Branch and Viral Carcinogenesis Branch, National Cancer Institute, Bethesda, Maryland 20014

A DNA polymerase that can copy RNA-RNA and RNA-DNA synthetic templates has been found in normal mouse and normal human cells. Partially purified polymerases from both sources have properties that are similar to those of the mouse leukaemia virus enzyme.

RNA dependent DNA polymerase activity¹⁻² has been found in all the known RNA-containing tumour viruses³⁻⁵ and in RNA-containing viruses not at present considered oncogenic, visna virus^{5,6} and "foamy" viruses^{5,7}. We have now detected and characterized RNA dependent DNA polymerase activity in cells known to contain such viruses. We have also found a similar RNA dependent DNA polymerase activity in uninfected murine and human cells. In addition, tumour cells from humans in which no known RNA-containing tumour virus has been detected contain polymerase activity.

Activity in Infected Cells

The use of double stranded synthetic RNA and RNA-DNA templates with manganese as the divalent cation greatly increases the sensitivity of detection of RNA dependent DNA polymerase activity in RNA-containing tumour viruses. In these conditions, as few as 10^2 - 10^3 infectious mouse leukaemia virions can be detected. To investigate the usefulness of such polymers in detecting viral RNA dependent DNA polymerase in cells, we used the double stranded RNA template, poly rA·rU, in two systems: mouse cells (BALB/3T3) transformed with the Moloney strain of murine sarcoma virus (M-MSV)⁸, and monkey kidney cells infected with a primate syncytium-forming virus (foamy virus type 3)⁷. As Fig. 1 shows, extracts of MSV-transformed BALB/3T3 readily polymerized ³H-TTP to the homopolymer deoxythymidylic acid (dT) by transcribing the adenylic acid strand of the poly rA·rU. Uninfected BALB/3T3 cells had detectable activity in these conditions. Similarly, extracts of primary African green monkey kidney cells infected with primate syncytium-forming virus ("foamy" virus) were able to polymerize ³H-TTP using poly rA·rU as the template, while control cells did not show enzyme activity (Fig. 2). The results demonstrate that RNA-dependent DNA polymerase activity can be found in crude extracts of cells that

are not tumour cells, if they contain a virus that has such a polymerase. In the case of the foamy virus-infected cells, this activity is present even though the cells are themselves producing only low levels of virus.

Because certain synthetic RNA-DNA hybrids are better templates than the RNA copolymer, poly rA·rU, for detecting the viral enzyme(s)^{3,4}, we examined uninfected and MSV-producing BALB/3T3 cells for activity using the hybrid template, poly rA·dT (Fig. 3). The riboadenylic acid strand was transcribed and ³H-TTP was polymerized into dT by transformed cell extracts. The activity per µg of protein was five to ten times higher than the corresponding activity detected with poly rA·rU. With poly rA·dT, however, uninfected BALB/3T3 extracts also demonstrated enzyme activity.

Enzyme Activity in Human Cells

Poly rA·dT dependent polymerase activity was examined in human diploid fibroblasts derived from skin biopsies of normal individuals and leukaemic cells obtained directly from patients with acute leukaemia. Fig. 4 shows one such example where crude extracts of normal fibroblasts incorporated ³H-TMP in response to poly rA·dT. The activity per µg of protein was somewhat higher in the leukaemic cells than in the normal fibroblasts in this case. But in other studies, levels of activity comparable with those in leukaemic cells have been found in lymphocyte cultures derived from normal individuals. While the levels of activity have varied, all human fibroblast and lymphocyte cultures from normal as well as tumoured individuals tested have shown this enzyme activity.

With crude cell extracts, at higher concentrations of protein, we found consistent inhibition of polymerase activity. This was particularly the case with the template poly rA·rU. We therefore partially purified the extract so as to characterize the requirements and template specificities of the cellular enzyme(s). Cell extracts were applied to a column of 'Sephadex G-200', and the fractions were assayed for polymerase activity (unpublished observations). The most active fractions were pooled and studied further.

The requirements for the polymerization of ³H-TTP in the presence of poly rA·dT with the partially purified cellular enzyme(s) from BALB/3T3 are shown in Table 1. Activity depended on polymer, enzyme, divalent cation, and time. Although less effective, magnesium could partially replace manganese as the divalent cation. The reaction was not significantly affected by the presence of the other three unlabelled deoxyribonucleoside triphosphates. Although the

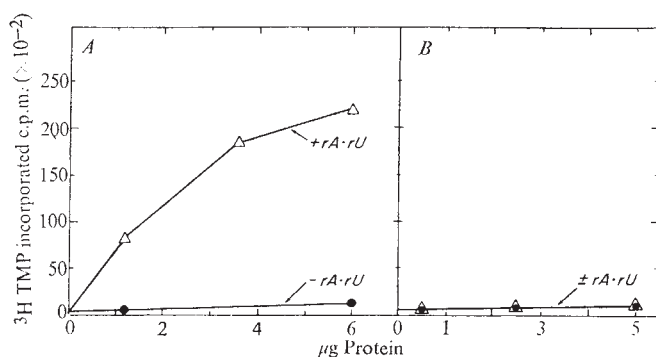


Fig. 1 Poly rA·rU dependent DNA polymerase activity in transformed BALB/3T3 fibroblasts. *A*, Moloney sarcoma virus-transformed line of BALB/3T3, MSV-BALB/3T3 Cl 1⁸, was the source of the transformed cell extract. This line produces approximately $10^{4.5}$ focus-forming units per ml. of MSV and $10^{6.2}$ plaque forming units per ml. of murine leukaemia virus (MuLV) as determined by the XC test²¹. *B*, Uninfected BALB/3T3 cell extracts. Cells were grown in 32 ounce glass prescription bottles in Dulbecco's medium with 10% calf serum (Colorado Serum Company). Two to four bottles were used for each extract. 2.5×10^6 cells were inoculated on day zero, the medium changed on day 2, and the cells collected on day 3. This procedure ensured 10^7 – 10^8 rapidly dividing cells for each extract. Cells were washed four times with 25 ml. in each wash of phosphate-buffered saline (PBS), scraped into 2.0 ml. PBS, and sedimented at 2,000 r.p.m. for five min. They were washed twice more by resuspending the cell pellet in 10 ml. of 0.05 M Tris-HCl, pH 7.8, 0.05 M potassium chloride, 0.001 M dithiothreitol (DTT) and 0.001 M manganese acetate (buffer A). A 2.0 ml. cell suspension (10^7 – 10^8 cells) was sonicated at 4° C for 1 min. An equal volume of saturated ammonium sulphate containing 0.05 M Tris-HCl, pH 7.8, and 1×10^{-4} M Na-EDTA was added. After centrifugation at 30,000g at 4° C for 20 min, the pellet was resuspended in 1.5 ml. of Buffer A without manganese acetate. 'Triton X-100' was added to a final concentration of 0.4% (v/v). The extract was incubated at 37° C for 15 min to release membrane-bound enzymes, centrifuged at 30,000g for 30 min at 4° C and the supernatant assayed. Protein was determined by the method of Lowry²². DNA polymerase was assayed as previously described⁵. Each reaction mixture was incubated at 37° C for 60 min and contained in 0.05 ml.: 0.02 M Tris-HCl, pH 7.8; 0.06 M potassium chloride; 0.001 M manganese acetate; 0.002 M dithiothreitol (DTT) 1×10^{-5} M; ^3H -TTP (5,000 c.p.m./pmol); 0.006 A₂₆₀ poly rA·rU and protein as indicated. ●, No polymer added; △, poly rA·rU added.

Table 1 Requirements for Uninfected BALB/3T3 Cell RNA-Dependent DNA Polymerase

Exp. 1A	^3H -TMP incorporated (c.p.m.)
Complete (Mn^{2+})	23,665
– Mn^{2+}	380
– rA·dT	215
– Enzyme	225
+ dATP	20,825
+ dATP, dCTP, dGTP	22,415
+ dATP, dCTP, dGTP	383
– rA·dT	
(zero time, complete)	(238)
Exp. 1B	
Complete (Mg^{2+})	5,730
– Mg^{2+}	320
– rA·dT	218
– Enzyme	236
+ dATP	5,325
+ dATP, dCTP, dGTP	5,720
+ dATP, dCTP, dGTP	320
– rA·dT	
Exp. 1C	
Complete (Mn^{2+})	636
– rA·dT	265

Each reaction mixture was incubated at 37° C for 60 min and contained in 0.05 ml.: 0.02 M Tris-HCl, pH 7.8, 0.002 M DTT; 0.04 M potassium chloride; and where indicated, 1×10^{-5} M ^3H -methyl-TTP (5,000 c.p.m./pmol); 1×10^{-5} M ^3H -dATP (5,000 c.p.m./pmol); 1×10^{-4} M each of unlabelled dATP, dCTP and dGTP; 3.0 µg of BALB/3T3 enzyme partially purified from the crude extract by 'Sephadex G-200' chromatography. The manganese acetate concentration in Exps. 1A and 1B was 1×10^{-3} M and the magnesium acetate concentration in Exp. 1C was 6×10^{-3} M. These concentrations were the optima for incorporation using poly rA·dT as the template. In Exp. 1C greater incorporation was not obtained with 1×10^{-4} M dATP (500 c.p.m./pmol).

incorporation of ^3H -TMP and ^3H -dCMP in response to two RNA-DNA hybrids, poly rA·dT or poly rI·dC, is shown in Table 3. All three enzymes incorporated ^3H -TMP in response to poly rA·dT but not in response to poly rI·dC. Conversely, ^3H -dCMP was incorporated in response to poly rI·dC but not in response to poly rA·dT. This demonstrates that incorporation of ^3H -TMP and ^3H -dCMP in response to RNA-DNA hybrids is consistent with transcription of the appropriate RNA strand rather than terminal addition to that RNA strand.

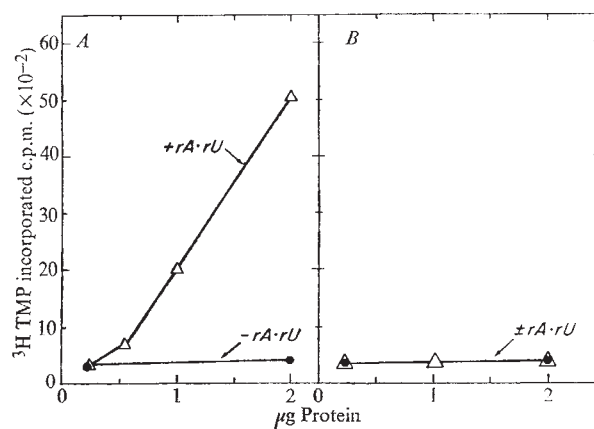


Fig. 2 Poly rA·rU dependent DNA polymerase activity in foamy virus infected primary African green monkey kidney cells. Primary African green monkey kidney cells (AGMK) were obtained from Microbiological Associates (Bethesda, Maryland). Each reaction mixture contained components as in the legend to Fig. 1. *A*, Infected 4 days previously with foamy virus type 3; *B*, uninfected AGMK. ●, No polymer added; △, poly rA·rU added.

riboadenylic acid strand was transcribed well, dAMP was incorporated poorly from the deoxythymidylic acid strand. In experiments not shown there was no detectable incorporation of either UTP or ATP.

Specificity of Viral and Cellular Enzymes

The template specificities of the polymerase activity of the partially purified enzymes from human fibroblasts, BALB/3T3 cells, and Rauscher murine leukaemia virus are compared in Table 2. All copied polyriboadenylic acid poorly and did not terminally add ^3H -TMP to a single stranded deoxythymidylic acid. The normal mouse and human cell enzyme(s), like the viral enzyme(s), were able to copy the rA strand of poly rA·rU. Of the three polymers, rA·dT, rA·rU and dAT, the RNA-DNA hybrid was the most active template for both the viral and cellular enzymes. Polymerase activities from two cases of human acute leukaemia were also examined for template specificity and have so far proved indistinguishable from the normal human fibroblast enzyme(s). Gallo *et al.*⁹ have reported a partially purified human leukaemia cell enzyme that can transcribe poly rA·rU.

Our studies show that neither the viral nor the normal cellular enzymes incorporate ^3H -TMP in response to single stranded RNA or single stranded DNA. They polymerize the deoxyribonucleoside triphosphate complementary to the RNA strand of an RNA-DNA hybrid. The specificity of

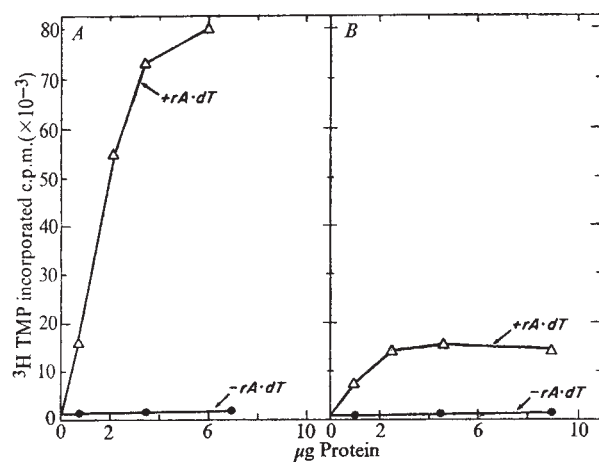


Fig. 3 Poly rA·dT dependent DNA polymerase activity in BALB/3T3 cells. Each reaction mixture was incubated at 37° C for 60 min and contained in 0.05 ml. components as the legend to Fig. 1 except poly rA·dT (0.006 A_{260}) was used in place of poly rA·rU. A, Transformed by Maloney sarcoma virus; B, control. ●, No polymer added; △, poly rA·dT added.

N-Demethylrifampicin inhibits the RNA dependent DNA polymerase activity of avian myeloblastosis virus¹⁰ and human leukaemic cell origin⁹. The effect of this inhibitor on the poly rA·dT dependent activity of the partially purified BALB/3T3 enzyme and the Rauscher leukaemia virus enzyme is shown in Table 4. Both enzymes were inhibited to a comparable degree by increasing concentrations of the antibiotic. Thus this particular inhibitor does not seem to distinguish between the viral and the cellular enzymes.

RNA Dependent DNA Polymerase in Cells

The levels of activity of RNA dependent DNA polymerase enzyme(s) in leukaemic cells are comparable with those found

Table 2 Template Specificity for RNA Dependent DNA Polymerase in Mouse and Human Fibroblasts

Source of enzyme	Template	Δ ^3H -TMP Incorporated (c.p.m.)
Rauscher virus (0.1 μg)	rA	< 50
	dT	< 50
	rA·rU	3,323
	rA·dT	52,223
	dAT	18,020
Mouse cells (BALB/3T3) (6.0 μg)	rA	123
	dT	133
	rA·rU	3,118
	rA·dT	53,925
	dAT	12,390
Human fibroblast (8SST) (4.0 μg)	rA	< 100
	dT	< 100
	rA·rU	1,270
	rA·dT	44,100
	dAT	20,560

For the viral and BALB/3T3 enzymes, each reaction mixture was incubated for 45 min at 37° C and contained in 0.05 ml. components as described in the legends to Fig. 1 and Table 1. All polymers were used at 0.006 A_{260} per 0.05 ml. Values in the absence of added template (200–250 c.p.m. for both viral and mouse cell enzyme) were subtracted from each determination. For the human cell enzyme each reaction mixture was incubated for 2 h at 37° C and contained identical concentrations of components except in 0.2 ml. The value in the absence of added template (1,040 c.p.m.) was subtracted from each determination. The higher value was due to the increased amount of ^3H -TTP in the 0.20 ml. rather than 0.05 ml. reaction. Reactions with the polymer dAT also contained 1×10^{-4} M unlabelled dATP. The Rauscher strain of murine leukaemia virus was obtained from plasma of infected mice as previously described⁵.

Table 3 RNA-DNA Hybrid Specificity for Viral and Cellular Enzymes

Source of enzyme	Template	Incorporation (c.p.m.)	
		^3H -TTP	^3H -dCMP
Rauscher virus (0.1 μg)	None	403	390
	rA·dT	66,523	320
	rI·dC	385	6,010
Mouse cell (BALB/3T3) (4.0 μg)	None	470	185
	rA·dT	33,221	225
	rI·dC	390	2,673
Human fibroblast (6.0 μg)	None	395	405
	rA·dT	25,240	500
	rI·dC	388	3,265

Each reaction mixture was incubated at 37° C for 60 min and contained in 0.05 ml. of 0.02 M Tris-HCl. pH 7.8; 0.04 M potassium chloride; 0.002 M manganese acetate; either 1×10^{-5} M ^3H -methyl-TTP (5,000 c.p.m./pmol) or 1×10^{-5} M dCTP (4,000 c.p.m./pmol); and either 0.01 A_{260} of rA·dT or rI·dC.

in lymphocytes derived from normal persons. The specificities for the synthetic templates so far tested also do not discriminate between normal and tumour cells. Therefore, the detection of this enzyme in human tumours in itself cannot be taken as evidence for the presence of an RNA-containing tumour virus in these cells. But the level of RNA dependent DNA polymerase activity in cells can be useful in certain well controlled situations to recognize virus-containing cells. Our studies show that polymerase activity is considerably greater in crude extracts from cells producing an RNA tumour virus or a foamy virus than it is in extracts from comparable normal cells. The cellular growth rate, stage of differentiation, cell type and various other factors may all affect the expression of polymerase activity. In cell culture using the model systems described here, many of these parameters can be controlled.

The finding of an activity in extracts of normal mammalian cells which can copy the RNA strand of poly rA·dT and the rA strand of poly rA·rU is analogous to the observations that DNA polymerase from *Escherichia coli* can transcribe both poly rA·rU¹¹ and natural RNA templates *in vitro*¹². We do not know whether the "reverse transcription" detected in extracts

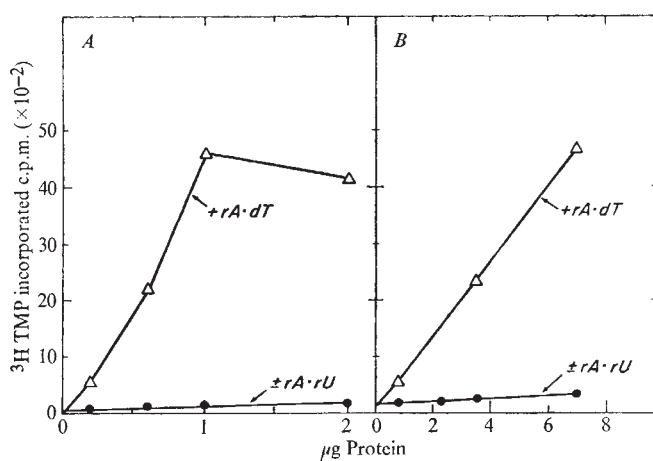


Fig. 4 Poly rA·dT dependent DNA polymerase activity in human leukaemic cells and human fibroblasts. A, Human leukaemic cells were obtained from the peripheral blood of an untreated young adult male with acute stem cell leukaemia, and a white blood count of 600,000/mm³ at the time of plasmapheresis. The cells were generously provided by Dr L. Dabisch (University of Michigan) as part of the Special Virus Cancer Program. The white cells were separated by centrifugation at 600g and stored in 15% DMSO at -170° C. B, Human fibroblasts were initiated from a punch biopsy from a normal volunteer. They were tested within five transfers of the initial explant. The cell strain tested (8SST) had no detectable virus as determined by sucrose density banding and had a normal susceptibility to both SV40 transformation and MSV transformation. Each 0.050 ml. reaction mixture was incubated at 37° C for 60 min and contained components as in Figs. 1 and 3.

Table 4 N-Demethylrifampicin Inhibition of Viral and BALB/3T3 Cell Enzyme Activity

Source of enzyme	Antibiotic ($\mu\text{g/ml.}$)	$^3\text{H-TMP}$ incorporated (c.p.m.)	% inhibition
Rauscher virus (0.1 μg)	None	25,280	—
	50	8,910	64
	150	825	98
	250	410	99
BALB/3T3 (4.0 μg)	None	36,605	—
	50	12,750	65
	150	1,250	97
	250	615	99

Each 0.05 ml. reaction mixture contained components as described in the legends to Fig. 1 and Table 2. Incorporation (230 c.p.m.) in the absence of rA-dT was subtracted from each value.

from presumably virus-free cells has a physiological role in bacterial and mammalian cells or is an artefact of the *in vitro* assay. Reverse transcription could play an important role in higher organisms, as Temin has pointed out¹³, in such critical functions as differentiation, antibody formation and memory.

Previous studies have shown that the viral polymerase is located in the core of the virus rather than being adventitiously absorbed¹⁴ and that many other RNA viruses show no such activity^{5,15}. These, along with a variety of biological studies^{16,17}, strongly suggest that the viral RNA dependent DNA polymerases play a physiological role in virus-infected cells.

The partially purified mouse cell enzyme has many properties in common with the leukaemia viral enzyme. Although further purification may well reveal differences, at present they have similar template specificities, are inhibited to a comparable degree by N-demethylrifampicin, and are not separable on the basis of size by 'Sephadex G-200' column chromatography (our unpublished observations). It is therefore possible that the polymerase of the RNA containing tumour viruses, like the replicase of the RNA bacteriophage, QB^{18,19}, contains host cell components. Whether the genetic information for making the enzyme resides in the virus, in the cell, or in both is unresolved.

BALB/3T3 is a continuous mouse cell line that is not tumorigenic. Other cell lines derived from the same embryo pool eventually did show expression of C-type virus informa-

tion²⁰. It could, therefore, be argued that the enzyme might be the only expression of latent viral genetic information in those cells. The similarity in properties described here between the mouse virus enzyme and the mouse cell enzyme would support this concept. But a similar enzyme is also found in human diploid cells—fibroblasts as well as lymphocytes. If all the enzyme activities we have described are manifestations of a latent viral genome, then it would seem to be ubiquitous.

We thank Drs David Baltimore, Howard Temin and Robert Wells for various polymers and suggestions, and Elaine Rands and Leslie Killeen for assistance. This work was supported in part by a contract from the National Cancer Institute.

Received January 5, 1971.

- Baltimore, D., *Nature*, **226**, 1209 (1970).
- Temin, H. M., and Mizutani, S., *Nature*, **226**, 1211 (1970).
- Mizutani, S., Boettiger, D., and Temin, H. M., *Nature*, **228**, 424 (1970).
- Spiegelman, S., Burny, A., Das, M. R., Keydar, J., Schlom, J., Travnick, M., and Watson, K., *Nature*, **228**, 430 (1970).
- Scolnick, E., Rands, E., Aaronson, S. A., and Todaro, G. J., *Proc. US Nat. Acad. Sci.*, **67**, 1789 (1970).
- Lin, F. H., and Thormar, H., *J. Virol.*, **6**, 702 (1970).
- Parks, W., Scolnick, E., Todaro, G. J., and Aaronson, S. A., *Nature* (in the press).
- Todaro, G. J., and Aaronson, S. A., *Virology*, **38**, 174 (1969).
- Gallo, R. C., Yang, S. S., and Ting, R. C., *Nature*, **288**, 927 (1970).
- Gurgo, C., Ray, R. K., Thiry, L., and Green, M., *Nature* (in the press).
- Lee-Huang, S., and Cavalieri, L. F., *Proc. US Nat. Acad. Sci.*, **50**, 1116 (1963).
- Cavalieri, L. F., and Carroll, E., *Biochem. Biophys. Res. Commun.*, **41**, 1055 (1970).
- Temin, H. M., *Persp. Biol. Med.* (in the press).
- Gerwin, B., Todaro, G. J., Zeve, V., Scolnick, E., and Aaronson, S. A., *Nature*, **228**, 435 (1970).
- Schlom, J., Burny, A., Harter, D., and Spiegelman, S., *Proc. US Nat. Acad. Sci.* (in the press).
- Temin, H. M., in *Biology of Large RNA Viruses* (edit. by Barry, R., and Mahy, B.) (Academic Press, New York, 1970).
- Bader, J. P., and Bader, A. V., *Proc. US Nat. Acad. Sci.*, **67**, 843 (1970).
- Kondo, M., Gallerani, R., and Weissman, C., *Nature*, **228**, 525 (1970).
- Kamen, R., *Nature*, **228**, 527 (1970).
- Aaronson, S. A., Hartley, J. W., and Todaro, G. J., *Proc. US Nat. Acad. Sci.*, **64**, 87 (1969).
- Klement, V., Rowe, W. P., Hartley, J. W., and Pugh, W. E., *Proc. US Nat. Acad. Sci.*, **63**, 753 (1969).
- Lowry, O. H., Rosebrough, N. J., Farr, A. L., and Randall, R. S., *J. Biol. Chem.*, **193**, 265 (1951).

Enterosecretory Proteins

by

JOEL W. ADELSON

Department of Biological Chemistry, Harvard Medical School, 25 Shattuck Street, Boston, Massachusetts 02115

The secreted vertebrate proteins, although widely divergent in function, have common biological and chemical features, including ontogeny in the enteroderm, a distinctive amino-acid composition and extensive similarities in amino-acid sequences. A unifying hypothesis could explain the evolution of these molecules and the glands which secrete them.

IN the evolution of the specialized tissues, ontogenesis and phylogenesis have been described by classical studies but the origin of tissue function at the biochemical level remains more uncertain because of the difficulties of studying biochemical function in a comparative fashion. It is possible, however, to throw light on the evolution of tissue function by examining the proteins synthesized and secreted by the differentiated tissues. In this article, I consider the secreted vertebrate proteins from two points of view—the embryology of the protein-secreting glands and the biochemical characteristics of the proteins themselves. The outcome is that many of the secreted proteins of vertebrates, although functionally different, are related to each other biologically and chemically. The

Table 1 Glandular Origins of some Protein Secretions and Embryological Origins of the Secretory Glands of Mammals

Secretion	Glandular origin of secretion	Character of secretion	Embryonic origin of gland
FSH, LH, prolactin, TSH, ACTH, GH, MSH	Anterior hypophysis	Hormones	Buccal ectoderm
Thyroglobulin, thyrocalcitonin	Thyroid	Hormones	Entoderm
Oxytocin, vasopressin	Hypothalamus	Hormones	Neural ectoderm
Salivary enzymes, mucoproteins, kallikrein	Salivary glands	Enzymes, mucins	Buccal ectoderm
Parathyroid hormone	Parathyroids	Hormone	Entoderm
Pepsinogen, gastrin, mucoproteins	Stomach	Enzyme, hormones	Entoderm
Many digestive enzymes, insulin, glucagon, kallikrein	Pancreas	Enzymes, hormones	Entoderm
Secretin, cholecystokinin, motilin	Duodenum	Enzymes, hormones	Entoderm
Peptidases, other digestive enzymes, mucus, substance P	Intestine	Enzymes, mucoid	Entoderm
Serum albumin, α and β globulins, prothrombin, fibrinogen, angiotensinogen, bradykininogen	Liver	Plasma factors, hormones, clotting factors	Entoderm
Renin, erythropoietin	Kidney	Enzyme	Mesoderm
Mucus proteins	Pulmonary tree	Mucoid	Entoderm
Reproductive fluid proteins	Bulbourethral, prostate	Mucoid	Entoderm
Milk proteins	Mammary	External secretion	Ectoderm
Relaxin	Corpus luteum	Hormone	Mesoderm
Gamma-globulins	Lymphocytes from thymus?	Antibodies	Entoderm?
Lysozyme	Avian egg, albumin, salivary, pancreas, lachrymal glands	Enzyme	Mesoderm, ectoderm, entoderm

FSH, Follicle stimulating hormone; LH, luteinizing hormone; TSH, thyroid stimulating hormone; ACTH, adrenocorticotrophic hormone; GH, growth hormone; MSH, melanocyte stimulating hormone.

Table 2 Amino-acid Composition of Selected Secreted and Nonsecreted Vertebrate Proteins

Amino-acid	Secreted (S) (percentage of total)	Nonsecreted (N)	S:N
Alanine	6.6	8.4	0.78
Phenylalanine	3.6	3.7	0.97
Lysine	7.0	7.6	0.92
Serine	8.2	4.9	1.68
Cystine	4.5	1.7	2.63
Glycine	6.1	5.8	1.05
Leucine	8.0	10.6	0.75
Proline	5.0	3.5	1.46
Threonine	6.4	4.7	1.39
Aspartic acid	7.5	8.3	0.90
Histidine	2.1	2.9	0.72
Methionine	1.6	2.4	0.67
Glutamine	3.9	2.9	1.35
Valine	6.4	5.0	1.27
Glutamic acid	8.8	15.2	0.58
Isoleucine	4.1	5.1	0.80
Asparagine	5.1	3.7	1.39
Arginine	3.4	5.9	0.57
Tryptophan	1.0	0.7	1.30
Tyrosine	3.8	3.2	1.19

The secreted vertebrate proteins chosen were trypsinogen, ribonuclease, melanocyte stimulating hormone, growth hormone, parathyroid hormone, fibrinopeptides A and B, chymotrypsinogen, elastase, pepsin, trypsin inhibitor, adrenocorticotrophic hormone, secretin, glucagon, insulin A and B chains, cholecystokinin, serum albumin, carboxypeptidase A, α -casein, β -lactoglobulin, luteinizing hormone, thyrotrophic hormone and ovomucoid. The non-secreted proteins were cytochrome C, cytochrome B5, haemoglobin, myoglobin, catalase, myokinase, adenosine triphosphate-creatine transphosphorylase, actin, myosin, lactic acid dehydrogenase, hyaluronidase, histone, glycogen phosphorylase, and apoferritin^{8,9}. Asparagine and glutamine were not determined in all the proteins included, thus the glutamic and aspartic acid percentages may be somewhat overestimated. The secreted group contained 3,306 amino-acids; the nonsecreted group contained 12,422 amino-acids.

proteins themselves seem to have originated among the digestive enzymes of earlier and simpler forms of life.

The basic mechanism for the evolution of the divergent molecules seems to have been duplication of genes coding for the proteins of the primitive digestive tract. Mutation and selection of the duplicated genes resulted in two kinds of further tissue differentiation. First comes the increasing specialization of regions of the digestive tract because of the evolution of new and divergent functions in the proteins

secreted. A less general train of mutational events seems to have been the activation in non-entodermal tissues of genes usually expressed exclusively in entoderm, and this seems to have led to the occasional production of secreted proteins by non-entodermal tissues. This article is a summary of the evidence available to support these hypotheses.

Origin of Secreted Proteins

Table 1 lists some proteins secreted by higher vertebrates, the tissue in which they are secreted and its embryonic origin¹⁻⁵. In spite of obvious omissions, the list represents the chief groups—enzymes, hormones, plasma factors and mucoid substances. Insoluble structural proteins such as collagen are, however, excluded. Plainly the great preponderance of the proteins listed arise in tissues which originate in the gut (entoderm or buccal ectoderm) during embryogenesis: and are thus derived from the gut of early pre-vertebrate species. The proteins secreted by these gut-derived tissues include all the digestive system proteins, nearly all the soluble blood proteins and many of the protein or peptide hormones. The entodermal tissues secrete at once a great amount of protein and a far greater functional variety of proteins than non-entodermal tissues. Although the latter synthesize organic molecules, their secretions are not, in general, proteins, but include steroids, catecholamines, mucopolysaccharides and other substances. The high degree of differentiation of the gut-derived tissues with respect specifically to protein secretion may be clearly contrasted with the lack of specialization of other tissues.

To be sure, protein secretions are not strictly confined to entodermal tissues, although there are few protein-secreting non-entodermal tissues which occur generally among the vertebrates. The only important exception is the hypothalamus of neural ectodermal origin, which secretes the cyclic peptides oxytocin and vasopressin and several hormone releasing factors. There are other non-entodermal protein-secreting tissues in specialized groups of animals which evolved long after the gut-derived glands and which include the mammalian corpus luteum, placenta and mammary gland; the metanephric kidney of mammals and birds, which secretes the proteolytic enzyme renin, and the skin glands of certain amphibia. As it happens, several of these non-entodermal protein secretions have chemical features which suggest that they are closely related to the secretion products of gut-derived tissues.

Enterosecretory Proteins

The common ontogeny of the protein-secreting glands implies that a limited group of gut proteins of earlier forms may have been the ancestors of many presently occurring secreted proteins, and this hypothesis is supported by several chemical observations. First, several secreted proteins of entodermal origin, including enzymes, hormones and clotting factors, are activated by a common mechanism involving the partial proteolytic digestion of a larger precursor resulting in the formation of smaller active products⁶. Among the molecules activated by this process are the proteinases, pepsinogen, chymotrypsinogen, trypsinogen, procarboxypeptidase, proelastase and prorennin; the blood clotting factors; and the hormones, proinsulin, thyroglobulin, angiotensinogen and bradykininogen. There is a highly developed mechanism of proteolytic cleavage in the case of fibrinogen; the action of thrombin on this precursor releases two active products, clot-forming fibrin and fibrinopeptide B, a hormone-like vasoconstrictor⁷.

in different species, such as the cytochrome *cs* or the insulins.) Paralogously related proteins, descended from a common ancestor, but with divergent functions in a single species—lysozyme and α -lactalbumin, for example—have not usually been characterized sufficiently well to be useful, although in due course they may be expected to provide a more general view of the changes which occur in protein structure and function during evolution.

Sequences suspected to have a paralogous relationship were tested by an empirical method, partly developed by Dayhoff and Eck¹⁴. Using the observed frequency of mutations occurring in known homologous proteins, they generated a "mutation probability matrix" for amino-acid sequences of 100 residues by imposing 256 accepted point mutations on a protein of average amino-acid composition. Sequences of suspected paralogous relationship were successfully tested by the chi square method for correspondence to this matrix with less than 256 accepted point mutations per 100 residues. "Homology" is used below only where the proteins have been success-

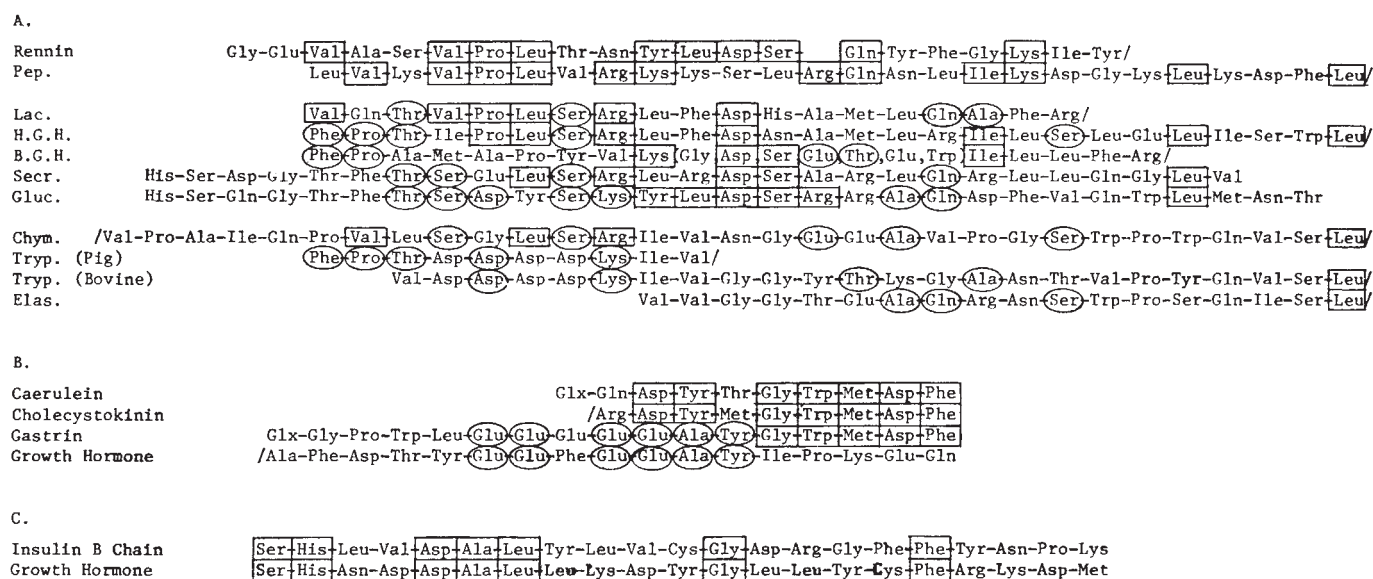


Fig. 1 Similarities between acid sequences of secreted protein and peptide enzymes and hormones. In group A, the amino-acids which are identical are enclosed in squares. The amino-acids which are identical to those in the corresponding position in the trypsin family are enclosed in ovals. In group B, the identities between gastrin and growth hormone are enclosed in ovals. The identities between caerulein, cholecystokinin, and gastrin are in squares. In group C, all identities are in squares. (/) indicates that the sequence is incomplete. Pep., Pepsinogen; Lac., lactogen; H.G.H., human growth hormone; B.G.H., bovine growth hormone; Ser., secretin; Gluc., glucagon; Chym., chymotrypsinogen; Tryp., trypsinogen; Elas., elastase.

The difference between the secreted and nonsecreted proteins is borne out by differences in amino-acid composition. Groups of secreted and nonsecreted vertebrate proteins of known amino-acid composition^{8,9} were used for the construction of two whole distributions (Table 2) which were then tested for similarity by the chi-square method with nineteen degrees of freedom. *P* was less than 0.01. The difference was mainly due to the relative abundance of serine and cystine and the relative scarcity of glutamic acid and arginine in the secreted group.

Further evidence for a common evolutionary origin is the similarity of the amino-acid sequences of several functionally very different secreted proteins. Two methods have been used to show homology between similar sequences. The method of Fitch, based on mutation distances between proteins, is readily subject to statistical interpretation, makes no assumptions about the likelihood of various types of mutation and requires no pre-alignment of amino-acid sequences, but the successful identification of homologous sequences requires either very long similar undelimited sequences or more closely related but shorter sequences¹⁰⁻¹³. (These criteria are met chiefly by orthologously related proteins with the same function

fully tested by the technique of Fitch; where the sequences pass only the empirical test, the term "similarity" is used.

Other cases of homology or similarity between secreted proteins include the homology among pancreatic chymotrypsinogen, trypsinogen and proelastase, and the similarity in several anterior pituitary hormones, including ACTH, MSH and β -lipotropin, each of which has a short identical section. The homology between pancreatic glucagon and duodenal secretin is noteworthy¹⁵, for the pancreas differentiates from the duodenum.

Similarities between proteins secreted by glands less ontogenically related than the pancreas and the duodenum are of potential interest in the study of the evolution of glandular function. A number of very similar sequences were found among the secreted proteins. Fig. 1A illustrates the N-terminal regions of four hormones secreted by pancreas (glucagon), duodenum (secretin), anterior hypophysis (growth hormone) and placenta (lactogen), and the N-terminal regions of five proteolytic enzymes. The hormones are similar to each other⁸ and, as a group, they are also similar to pepsinogen and rennin from stomach. They are less similar to the homologous pancreatic proteinases, chymotrypsinogen, trypsinogen and

elastase. With the exception of placental lactogen, all these proteins are secreted by tissues which originate in the embryonic gut. The high degree of similarity between the hormones and the digestive enzymes indicates a common origin. This represents the widest functional divergence yet observed among paralogously related protein molecules and may have important relevance to the mechanism of action of these hormones and the manner in which such mechanisms have evolved.

It has been noted that the C-terminal regions of the hormones gastrin (stomach), cholecystokinin (duodenum) and the amphibian ectodermal peptide caerulein are identical. In addition, gastrin and human growth hormone both possess a

been placed within the sequences wherever necessary to maintain maximum similarity⁸. Such gaps were originally placed by the investigators who formulated the internal arrangement of each group. Two additional gaps have been placed in group I and nine in group II. Of the 109 positions occupied by both groups, there are fifty-one cases of inter-group identities. There are six positions where all five amino-acids are identical. These are leucine 26, threonine 47, cystines 71, 87 and 108, and tryptophan 152. In seven positions, four of the five residues are identical; these occur at a leucine, a proline, two serine, a glycine, an isoleucine and a valine residue. Of the fifty-one instances of identical amino-acids in groups I and II

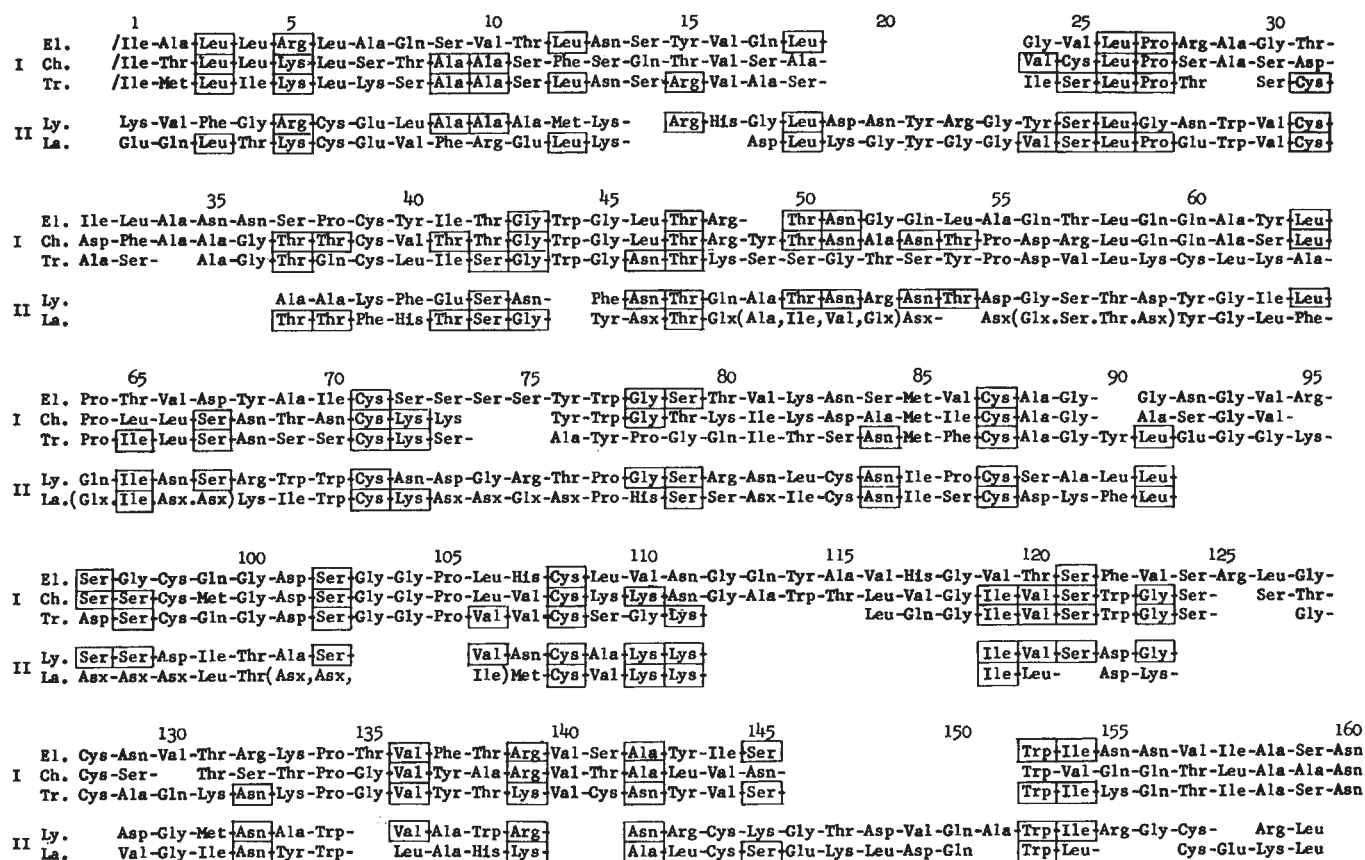


Fig. 2 Similarities between amino-acid sequences of three proteinases (group I), and lysozyme and lactalbumin (group II). El., Elastase; Ch., chymotrypsinogen; Tr., trypsinogen; La., α -lactalbumin; Ly., lysozyme. Positions in the trypsin family which are identical to La. and/or Ly. are enclosed in squares. The N-terminal regions of the trypsin family have been omitted; El., Ch., and Tr. begin with the 94th, 103rd, and 91st residues, respectively.

short section in which six out of seven positions are identical (Fig. 1B). A similarity in sequence between human growth hormone and an "ancestral insulin" can be seen in Fig. 1C. The insulin sequence was generated by computing the most probable antecedent amino-acid sequence of the known insulins⁸. Growth hormone and insulin are closely related in their physiological effects. A cyanogen bromide-cleaved section of bovine growth hormone, which contains this insulin-like sequence, exhibits an insulin-like activity on the rat epididymal fat pad incorporation of glucose into fatty acids¹⁶. Thus at least four different gut-derived glands—stomach, pancreas, duodenum and anterior hypophysis—secrete proteins which are similar to different sections of the growth hormone.

Sequences from two functionally distinct groups of secreted enzymes are shown in Fig. 2. Group I consists of the homologous proteases, elastase, trypsin and chymotrypsin; group II consists of the homologues egg white lysozyme and α -lactalbumin. Only the C-terminal portions of the trypsin family are shown. Gaps representing insertions or deletions have

in a given position, forty-three of these include three or more of the possible five positions, indicating that an amino-acid conserved in group I also tended to be conserved in group II. A further similarity occurs at the structural level: the cystine residues in positions 71 and 87 form a disulphide bridge in all five enzymes. The similarity in the sequences of the two groups provides an example of an evolutionary relationship between two different protein families, and represents the widest divergence in enzymic function found to date among enzymes of common origin.

A specialized non-entodermal mammalian secretion, α -lactalbumin, occurs in milk. Its site of synthesis has not been found. Lysozyme occurs in both entodermal and non-entodermal secretions¹⁷. Both enzymes function in the metabolism of β -1-4-glucosidic linkages. The active sites of the proteinases of group I are not located in the section of the protein similar to group II (refs. 8, 18, 19). Current ideas about the mechanism of protein evolution imply that the accumulation of a large number of mutations in the descendants of a protein-coding gene eventually leads to proteins which bear less structural and

little or no functional resemblance to the ancestral protein. Empirically, this concept is supported only in cases in which evolution has led to families of protein of common function, for example, the cytochrome *cs* and the trypsin family. The sequences presented in Figs. 1 and 2 represent a greater degree of divergence of function; in several cases the isolated sequences have no common biochemical or physiological function. It may be proposed from the above sequences that certain protein hormones originated from digestive proteolytic enzymes of simpler species of provertebrates, and that the lysozyme and trypsin families of enzymes share a common ancestor.

Origin of Glands and Proteins

The observations cited so far to support the hypothesis that the secreted vertebrate proteins, as well as their glands of origin, are biologically and chemically related to each other are (1) ontogeny in the digestive tract, (2) the proteinaceous character of endodermal secretions, (3) the large functional variety of endodermal secreted proteins relative to other tissue precursors; (4) the partial proteolytic activation mechanism widespread among endodermal proteins; (5) the distinct amino-acid compositions; (6) related amino-acid sequences; and (7) the close relationship between amino-acid sequences among endodermal and rarely occurring non-endodermal proteins. Furthermore, Eylar²⁰ has shown that secreted proteins are often glycoproteins. All support the following integrated hypothesis concerning the genesis of function in vertebrate protein secreting glands: the serine proteinases, found in a bacterium *Sorangium* sp.²¹, occurred at the unicellular or prokaryotic period and became localized as the digestive tract developed. The gastric filaments of the coelenterate sea anemone *Metridium senile* contain chymotrypsin-like enzymes²². The serine proteinase did not necessarily develop simultaneously with the extracellular secretion process. Protozoa and porifera have a vacuolar, intracellular digestive process²³. As the cells associated to form the digestive tube, the extracellular secretion process, typical of higher forms, become prevalent.

It may be assumed that the primitive digestive tract secreted a limited number of enzymes, having no regions of anatomical specialization. Mutation and selection of genes coding for the simple primitive gut gave rise to related families of digestive enzymes with different functions; a contemporary example is the trypsin family. The principal genetic mechanism making this divergence possible was gene duplication²⁴. It enabled simultaneous encoding of an original protein from two separate genes and subsequent divergent mutations in each gene. Duplication and mutation of genes, and changes in the time and location of the expression of the genes in the developing organism, account for the homology²⁵ between the exocrine pancreatic trypsin family and the endocrine hepatic prothrombin molecule.

The genetic changes in the time and location of expression of the functionally different, related genes led to the evolution of functionally specialized regions of the gut; enlargement of these regions led to the development of specialized tissues and eventually organs. The ability to secrete related proteins remained constant among the gut-derived glands. To a lesser extent, the mechanism of partial proteolytic activation of secreted products was also retained. The variety of physiological functions served by the secreted proteins increased greatly as new varieties of related proteins evolved. When enough sequences of enterosecretory proteins are available, the basic concepts of a phylogeny of the tissues may be developed.

An interesting and somewhat obscure mechanism led to the ability of several specialized non-endodermal tissues to secrete proteins related to endodermal proteins such as caerulein, lysozyme, α -lactalbumin and placental lactogen. Again the basic mechanism was gene duplication, followed either by a physical translocation of a copy of the gene into another, non-endodermal, section of the genome. Alternatively, a change in the pattern of gene-activation occurred, allowing expression

of a formerly repressed endodermal gene in a non-endodermal tissue.

Enterosecretory System

The embryonic entoderm has long been recognized as the progenitor of several secretory tissues. Unlike the secretions of tissues from other sources, endodermal derivatives are nearly all proteins and they have a wide variety of functions. Barrington²⁶, the first to try to explain the evolution of thyroid and parathyroid function, used an integrated phylogenic-ontogenic approach. Later, Geschwind²⁷ used a combined protein chemistry-physiological approach to the evolution of several peptide hormones. Information about protein structure and the recognition of the protein-secretory capability of entoderm has made it possible for us to extend, in outline, the explanation of evolutionary development of physiological function in the protein-secreting tissue. The digestive enzymes of simple invertebrates contain a great deal more information about the evolution of biological function.

One more physiological implication may be mentioned. A number of tissues with both exocrine and endocrine secretory functions—for example, the liver, lungs, intestine and stomach—are derived from the entoderm. It is embryologically and biochemically reasonable to refer to a "vertebrate enterosecretory system", this being a group of tissues derived from embryonic gut which secretes extracellular proteins and transports metabolic substrates such as oxygen into the organism.

I thank Professor E. R. Blout for encouragement; Drs W. M. Fitch, D. Torchia and P. Holland for help with statistical analysis, and Drs A. Rich, S. S. Rothman, R. E. Fine, H. M. Goodman, T. H. Wilson, M. Soodak, L. Visser, Messrs B. L. Bowman, A. Brush, and S. Abramson for criticism. The work was supported by the US Public Health Service and the National Cystic Fibrosis Research Foundation.

Received July 17; revised October 1, 1970.

- ¹ White, A., Handler, P., and Smith, E. L., *Principles of Biochemistry*, fourth ed. (McGraw-Hill, New York, 1968).
- ² Arey, L. B., *Developmental Anatomy* (Saunders, Philadelphia, 1965).
- ³ Patten, B. M., *Human Embryology*, third ed. (Blakiston, New York, 1969).
- ⁴ Florey, E., *General and Comparative Animal Physiology* (Saunders, Philadelphia, 1966).
- ⁵ Jenkins, P. M., *Animal Hormones* (Pergamon, Oxford, 1962).
- ⁶ Ottensen, M., *Ann. Rev. Biochem.*, **36**, 55 (1967).
- ⁷ Colman, R. W., Osbahr, A. J., and Morris, R. E., *Nature*, **219**, 292 (1967).
- ⁸ Dayhoff, M. O., *Atlas of Protein Sequence and Structure* (Nat. Biomed. Res. Foundation, Maryland, 1969).
- ⁹ Tristram, G. R., and Smith, R. H., *Adv. Protein Chem.*, **18**, 227 (1963).
- ¹⁰ Margoliash, E., and Fitch, W. M., *Ann. NY Acad. Sci.*, **151**, 359 (1968).
- ¹¹ Fitch, W. M., and Margoliash, E., *Brookhaven Symp. Biol.*, **21**, 217 (1968).
- ¹² Fitch, W. M., *J. Mol. Biol.*, **16**, 9 (1966).
- ¹³ Fitch, W. M., *Biochem. Genetics*, **3**, 99 (1969).
- ¹⁴ Eck, R. V., and Dayhoff, M. O., *Atlas of Protein Sequence and Structure*, 33 (Nat. Biomed. Res. Foundation, Maryland, 1967).
- ¹⁵ Jorpes, J. E., *Gastroenterology*, **55**, 157 (1968).
- ¹⁶ Nutting, D. F., Kostyo, J. L., Goodman, H. M., and Fellows, jun., R. E., *Endocrinology*, **86**, 416 (1970).
- ¹⁷ Jollès, P., in *The Enzymes* (edit. by Boyer, P., Lardy, H., and Myrback, K.), (Academic Press, New York, 1960).
- ¹⁸ Jansen, E. F., Nutting, F., Jang, R., and Balls, A. K., *J. Biol. Chem.*, **179**, 189 (1949).
- ¹⁹ Smillie, L. B., and Hartley, B. S., *Biochem. J.*, **101**, 232 (1966).
- ²⁰ Eylar, E. H., *J. Theoret. Biol.*, **10**, 89 (1966).
- ²¹ Kaplan, H., and Whitaker, D. K., *Canad. J. Biochem.*, **47**, 205 (1969).
- ²² Gibson, D., and Dixon, G. H., *Nature*, **222**, 753 (1969).
- ²³ Villee, C. A., Walker, jun., W. F., and Smith, F. E., *General Zoology* (Saunders, Philadelphia, 1958).
- ²⁴ Nei, M., *Nature*, **221**, 40 (1969).
- ²⁵ Magnusson, S., *Biochem. J.*, **110**, 25p (1968).
- ²⁶ Barrington, E. J. W., *Hormones and Evolution* (English Universities Press, London, 1964).
- ²⁷ Geschwind, I. I., *Amer. Zoologist*, **7**, 89 (1967).

LETTERS TO NATURE

PHYSICAL SCIENCES

Circular Components of Polarization in Pulsar Radiation

INDIVIDUAL radio pulses from many pulsars have been found to be highly polarized. Pulses from PSR 0329 contain a large circular component¹, so that the polarization is generally elliptical, but the handedness of the circular component appears to be variable, so that the Stokes parameter V changes in sign both during an individual pulse and from pulse to pulse. If this variation were completely random, then an integrated profile of V obtained by summing several hundred pulses would be close to zero. The Stokes parameters Q and U , on the other hand, representing linear polarization, do not sum to zero in this way and large average linear polarizations are

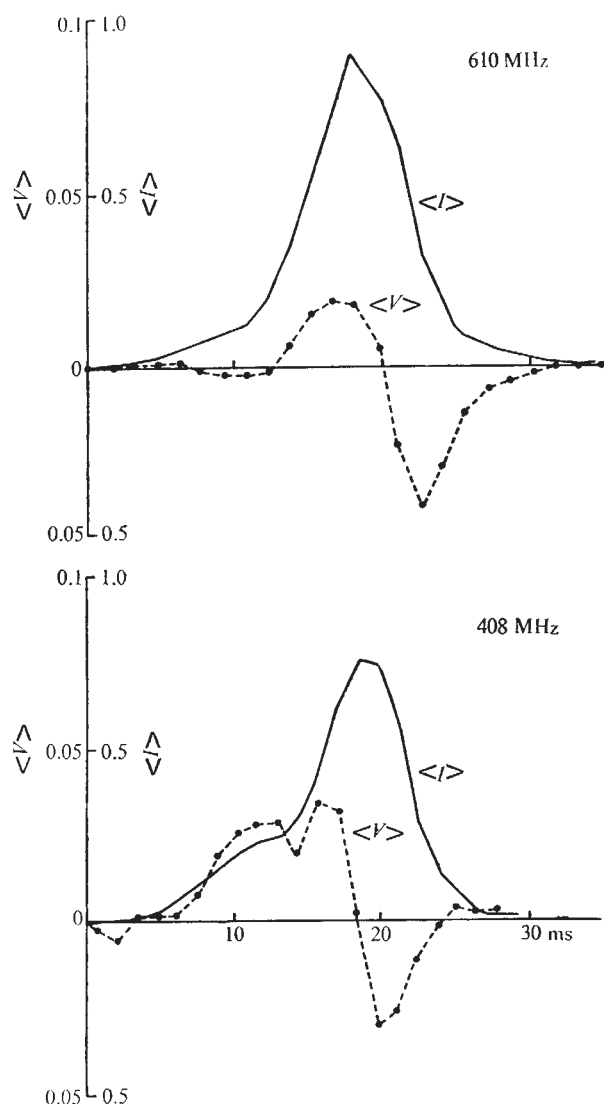


Fig. 1 Integrated intensity $\langle I \rangle$ and circular polarization $\langle V \rangle$ of pulses from CP 0329 at: (a) 610 MHz; (b) 408 MHz.

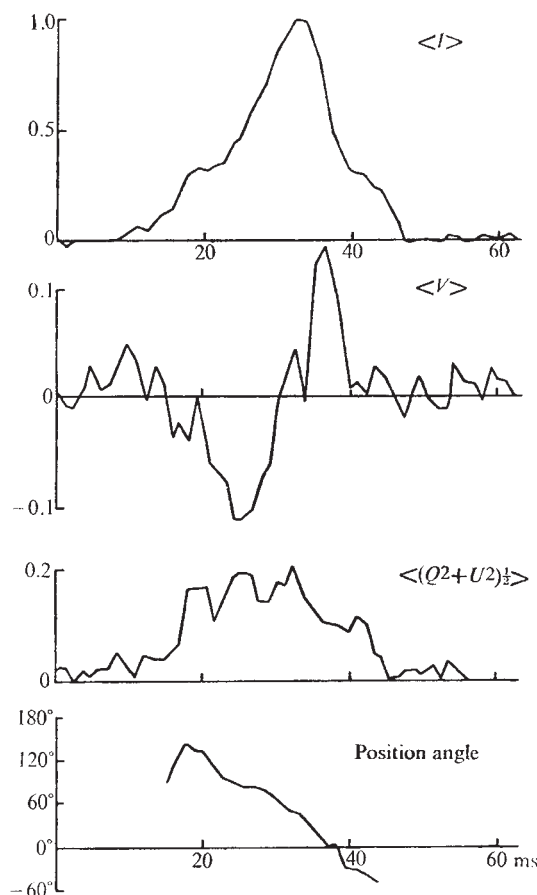


Fig. 2 The polarization of integrated pulses from PSR 1508 at 408 MHz, showing intensity $\langle I \rangle$, circular polarization $\langle V \rangle$, linear polarization $\langle (Q^2 + U^2)^{1/2} \rangle$ and position angle Φ .

observed in many pulsars²⁻⁵. So far, however, only one observation² of one pulsar (PSR 1749) suggests that the average V profile is significantly different from zero. In an extended series of observations, we now find that the average V component is significantly different from zero in many pulsars, although it seldom approaches the strength of the linear component $\langle (Q^2 + U^2)^{1/2} \rangle$. The average V component is particularly strong in the pulsars PSR 0329 and PSR 1508.

Observations were made with 1.5 MHz bandwidth at 610 MHz. The parameter V was obtained by correlating in the appropriate phase the outputs of two orthogonal dipoles at the focus of the Mark I telescope. Fig. 1a represents an integration over 5 min, showing the average $\langle V \rangle$ with the average intensity $\langle I \rangle$, and $\langle V \rangle$ is seen to reverse during the profile, reaching about 15% and 25% of $\langle I \rangle$ before and after the reversal. This pattern can be seen in many individual pulses, but with considerably higher degrees of circular polarization.

Fig. 1b shows a similar recording of V at 408 MHz with a 300 kHz bandwidth. In this measurement a quite different polarimeter system was used in which V was obtained by direct subtraction of left and right circular components formed by a hybrid connexion at the dipole feed. The errors in these

observations due to coupling between the I and V detectors are therefore independent, but they may amount to 5% at 408 MHz and almost 3% at 610 MHz.

The two recordings are very similar. Both show a left circular component followed by a right circular component, with similar pulse shapes and degrees of polarization.

Recordings of PSR 1508 obtained at 408 MHz are shown in Fig. 2, which displays the average linear polarization (average about 15%) as well as the circular polarization, which amounts to 30% at maximum. The position angle of the polarization ellipse sweeps approximately linearly through 180° in this pulsar.

Out of eighteen other pulsars from which good recordings were obtained, at least ten show a component of $\langle V \rangle$ which reaches 10% or more at some part of the pulse profile. In two which show a profile with a double peak (PSR 0834 and PSR 1133) there is a component of $\langle V \rangle$ amounting to about 10% but with opposite hands in the two halves of the pulse.

The organized part of the circular polarization is now seen to be a general property of pulsar radiation. Further, the present observations of PSR 0329 at 408 MHz and 610 MHz may be combined with observations⁶ of single pulses at 240 MHz and 408 MHz to show that this phenomenon is practically independent of frequency, as is the organized part of the linear polarization.

D. A. GRAHAM

University of Manchester,
Nuffield Radio Astronomy Laboratories,
Jodrell Bank

Received November 12, 1970.

¹ Clark, R. R., and Smith, F. G., *Nature*, **221**, 724 (1969).

² Ekers, R. D., and Moffett, A. T., *Ap. J.*, **158**, 11 (1969).

³ Komesaroff, M. M., Morris, D., and Cooke, D. J., *Astrophys. Lett.*, **5**, 37 (1970).

⁴ Morris, D., Schwarz, U. J., and Cooke, D. J., *Astrophys. Lett.*, **5**, 181 (1970).

⁵ Manchester, R. N., *Nature*, **228**, 264 (1970).

⁶ Smith, F. G., *Nature* (in the press).

Evidence of Foundered Continental Crust beneath the Central Tyrrhenian Sea

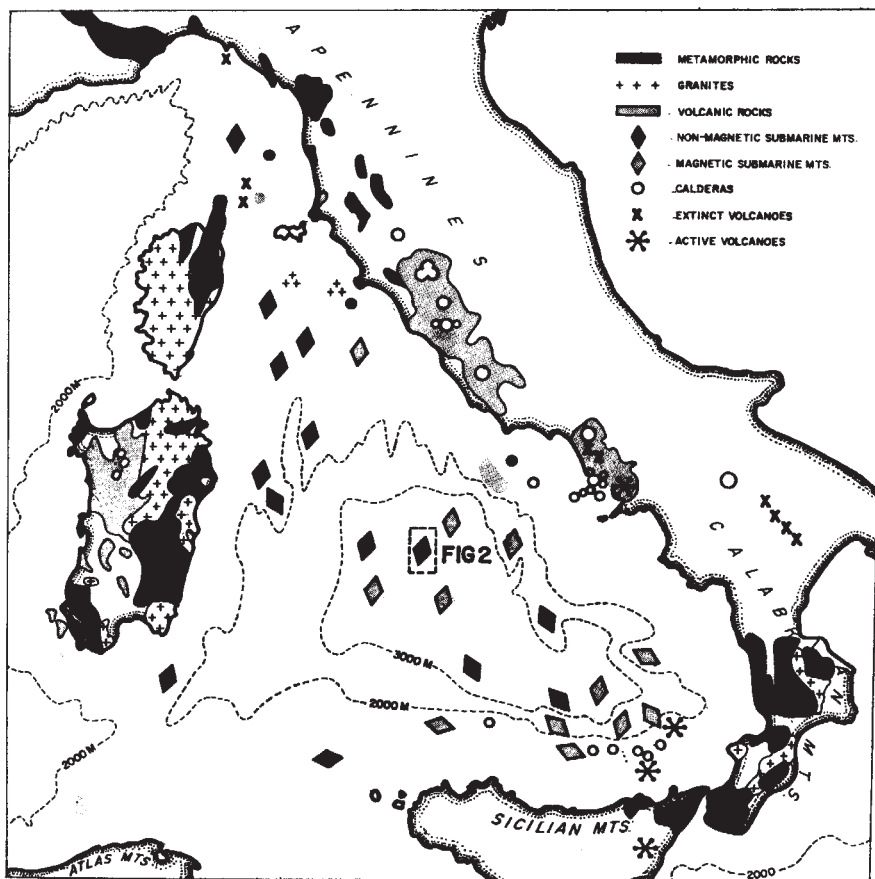
THE dredging of schists, phyllites and marbles from the faulted margin of a tilted crystal block in the central Tyrrhenian Sea shows that the acoustical basement beneath the centre of this sea basin includes a sequence of rocks similar or perhaps identical to the Palaeozoic and Triassic schists and phyllites of the adjacent Apennine, Calabrian and Sicilian chains, the Pontian Islands¹ and Sardinia. Even the low to medium grade metamorphism observed must have occurred beneath the Earth's surface and following metamorphism and deformation we infer that these rocks were uplifted, denuded by sub-aerial erosion and finally foundered more than 3,000 m below sea level. The Neogene subsidence is still continuing. The metamorphic rocks obtained from the Tyrrhenian acoustic basement appear to support the former existence of the Tyrrhenides and indicate that this ancient upland was underlain by continental crust.

The central Tyrrhenian Sea occupies an important depression in the Earth's surface which is located between the ancient Hercynian schists of Sardinia³ and the belt of Tertiary deformation which includes the Apennine, Calabrian and Sicilian chains of Italy and their Hercynian nuclei^{4,5}, as well as the Atlas Mountains of Africa (Fig. 1). It has often been postulated that the Tyrrhenian Sea basin, now more than 3,000 m deep, is the site of a former continental land mass (the Tyrrhenides) which subsided beneath the sea in Neogene times⁶.

This hypothetical foundered land has been invoked to explain late Tertiary vertebrate distributions and cited as the source of some Tertiary clastic sediments including exotic blocks of crystalline rocks in the Apennine (Oligocene) and Atlas chains.

Little is known about the composition of the Earth's crust beneath the Tyrrhenian Sea, but published seismic refraction measurements⁷⁻⁹ indicate the presence of crustal layers possessing compressional wave velocities of 4.0, 5.0, 5.7 and 7.1

Fig. 1 Metamorphic rocks of the Tyrrhenian region.



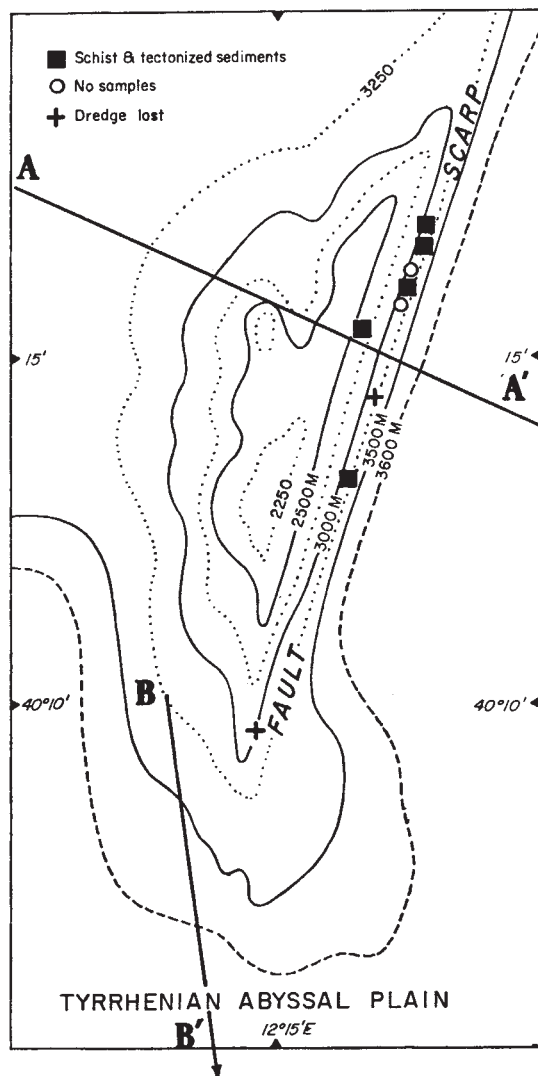


Fig. 2 Basement outcrops on a tilted fault block in the central Tyrrhenian Sea. Topography based on a survey by RV Bannock⁹.

km s⁻¹. Linear magnetic anomalies considered by some to be similar to those of the Mid-Oceanic Ridge have also been reported¹⁰. Some investigators have interpreted the geophysical results in terms of the presence of oceanic crust beneath the Tyrrhenian Sea and have thus cast doubt on the foundered continent hypothesis. Separation of Sardinia from Italy by opposed crustal drift with the simultaneous creation of the Tyrrhenian Sea floor through axial accretion has been suggested as an alternative to foundering¹¹. The latter hypothesis which proposes an oceanic type Tyrrhenian crust would, in essence, make Sardinia the site of the Tyrrhenides¹².

The topography of the Tyrrhenian Sea floor is marked by a linear system of ridges and troughs oriented approximately N 15° E (refs. 13 and 14). Several of these ridges rise to heights of one or two thousand metres above the adjacent seafloor as linear seamounts. Some are marked by large magnetic anomalies (Fig. 1) and volcanic rocks have been sampled from a number of them¹⁵; other linear ridges possess no magnetic anomaly and appear to be entirely tectonic. One sharply asymmetrical ridge near the north-west edge of the Tyrrhenian abyssal plain^{16,17} was investigated in August 1970 on a cruise of RV Atlantis II (Fig. 2). The magnetic field over this ridge is relatively smooth and lacks the typical large anomalies characteristic of volcanic peaks (Fig. 3). The seismic reflexion profiler recorded no sediment from the eastern escarpment, and the narrower beam echo sounder failed to record any echoes from a large proportion of the precipice. The scarp was

dredged seven times but only five hauls were successful (Fig. 2).

The rocks dredged are of three general types: (1) metamorphic rocks, namely, crystalline schist, phyllite and marble; (2) sedimentary rocks showing signs of considerable deformation and fracturing; and (3) undeformed fossiliferous limestones.

The schists are of low to medium metamorphic grade, and the principal minerals are quartz, chlorite and sericite; biotite, calcite and magnetite are also present. Schistosity is well developed in most of the specimens. Bedding lamination is suggested by quartz silt and calcite layers visible in many of the specimens; a few also show kinking of the schistosity at a sharp angle to the primary foliation.

Several specimens are massive magnetite, and intercalated thin layers of muscovite-quartz show that this magnetite represents a layer in the schist which probably contains at least 50% iron. One small piece of grey schistose marble composed of calcite with biotite and amphibole has been found and probably represents a high lime layer in the schist. Among the rocks showing signs of deformation, but no real metamorphism, are siltstones, limestones and dolostones. The siltstones and limestones break along bedding or bedding laminations but both show faint cleavage at an angle to the bedding. The limestones have a fine sugary texture and disintegrate easily, apparently because of weathering; they resemble limestones which have been recrystallized because of intense folding. The dolostone has a crystalline texture and is from a bed about 10 cm thick. It is extensively fractured and veined with calcite and dolomite. One piece of siltstone shows no tectonic fabric but is peppered with small grains of magnetite (partially altered to limonite). This magnetite is evenly distributed throughout the specimen and is apparently not detrital; it may have formed as the result of metamorphism (contact or regional) of a ferruginous sediment.

The foraminiferal limestones are completely different in appearance; they are pale buff in colour, and aphanitic or finely crystalline with conchoidal fracture. All specimens have been burrowed and in some cases the borings have been filled with a consolidated mixture of foraminifera tests and pteropod fragments. Most specimens were found with a thin coating of manganese oxide (~1 mm). The larger specimens have fresh surfaces where they had apparently been broken away from an outcrop.

The rocks, which were sampled, crop out on a tilted crustal block, extending from the base of the escarpment at 3,600 m to within a few hundred metres of its top at 2,200 m (Fig. 3A). Regional metamorphism implies moderately deep burial and thus, in this case, subsequent erosion. Submarine erosion processes are not considered sufficient to remove thousands of metres of consolidated rock and therefore the presence of metamorphic rocks so near the top of the escarpment points to subaerial erosion. The date of the submergence of the eroded basement cannot be estimated from our samples, but the presence throughout the deep Tyrrhenian basin of only 200 to 400 m of sediment¹⁸ would in any case suggest that the marine deposits of the Tyrrhenian Sea represent no longer a period than Neogene time. The continuation of the subsidence at the present time can be inferred from the manner in which successively younger turbidite layers detected with the seismic reflexion profiler become thinner towards the south flank of the tilted fault block (Fig. 3B).

We come to the conclusion that a continental terrain formerly existed in the present location of the Tyrrhenian Sea and that it started to subside during Neogene time. The subsidence of the Tyrrhenides appears to have been accompanied, and perhaps caused, by extension of the crust which broke the former continental crust into a series of crustal slivers which are now represented by narrow ridges. Volcanic activity along these same faults created the linear volcanic piles of the south-east Tyrrhenian Sea.

If the dredged schists correspond in age to similar rocks of the adjacent lands (Fig. 1), they would not only constitute the

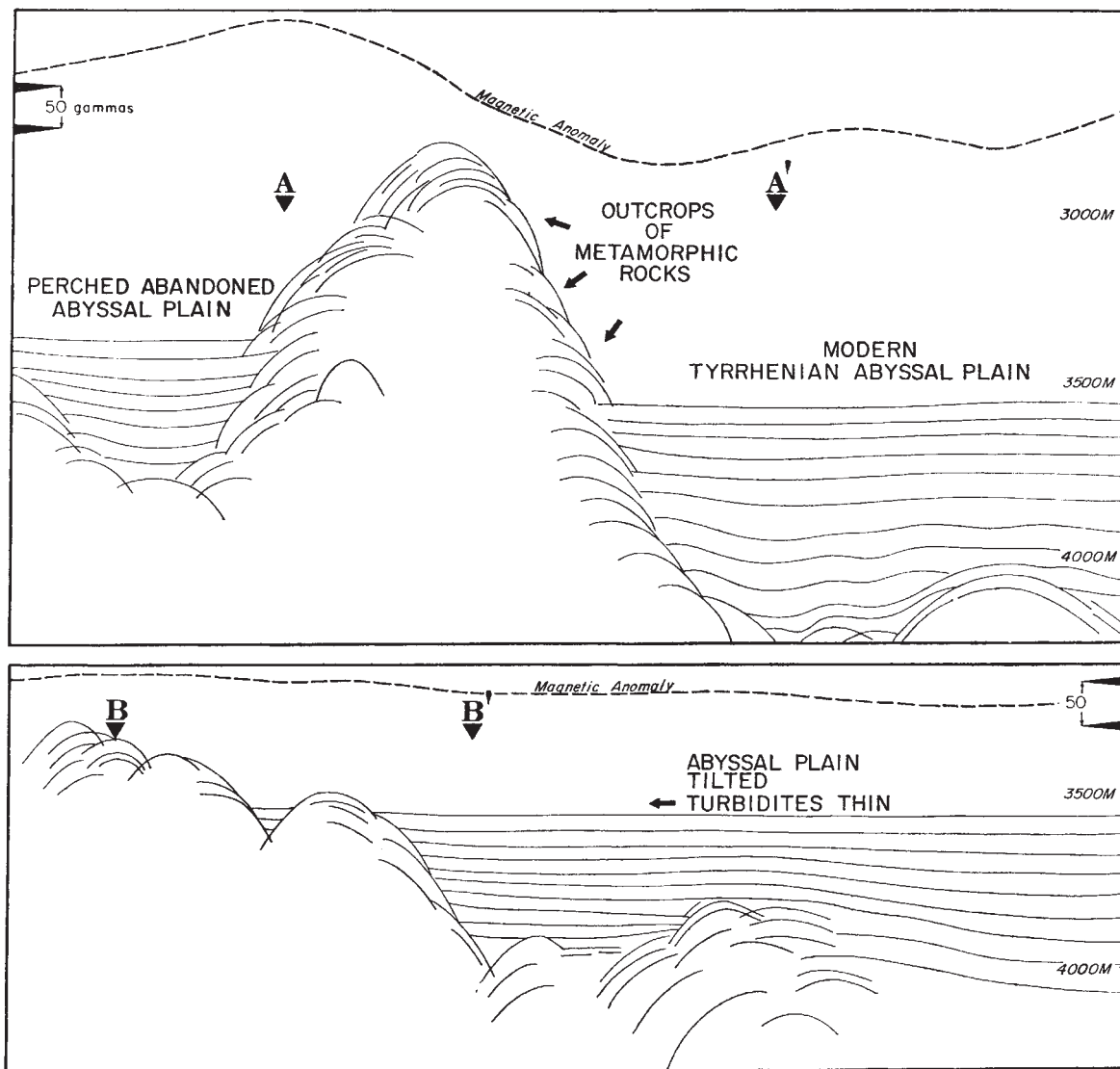


Fig. 3 Seismic reflection profiles across the tilted fault block (see Fig. 2). A 40 inch³ air gun was used as an acoustic source. Anomalies of total magnetic intensity were determined with a proton precession magnetometer. Turbidites of the Tyrrhenian abyssal plain (A) show Quaternary deformation. Pondered turbidites (B) of the abyssal plain become thin towards the positive fault block.

oldest rocks so far obtained from the deep seafloor¹⁹⁻²¹ but might provide the first direct evidence that foundered Mesozoic and Palaeozoic continental crust exists beneath the Mediterranean Sea.

Cruise 59 III of Atlantis II was supported by a US National Science Foundation grant and was part of the US-Italy Cooperative Oceanographic Program. We thank G. Almagor, W. Cotton, A. Jefferson, W. Kanes, J. Levy, D. Neev, T. O'Brien, M. Palmeri, J. Pike, R. Robbins, C. Robin, C. Scott, P. Teti, A. Williams and H. K. Wong for assistance at sea.

B. C. HEEZEN

Lamont-Doherty Geological Observatory,
Columbia University, New York

C. GRAY

Faculty of Science, University of Libya, Tripoli

A. G. SEGRE

Istituto Geologia, University of Messina

E. F. K. ZARUDSKI

Woods Hole Oceanographic Institution,
Woods Hole, Massachusetts

Received October 12, 1970.

¹ Segre, A. G., *Memorie Soc. Tosc. Sci. Nat.*, **75**, 231 (1968).

² Segre, A. G., *Accad. Naz.*, **40**, 76-77 (1953-54).

³ Ferrara, G., Segre, A. G., and Tongiorgi, E., *Memorie Atti. Soc. Tosc. Sci. Nat. A.*, **69** (1962).

⁴ Ferrara, G., and Longinelli, A., *Bull. Soc. Geol. Ital.*, **80** (1961).

⁵ Borsi, S., Ferrara, G., Rau, A., and Tongiorgi, M., *Memorie Atti. Soc. Tosc. Sci. Nat. A.*, **63** (1955).

⁶ *Symposium on Oceanization of the Western Mediterranean*, **26** (Royal Netherlands Geol. Min. Soc., 1969).

⁷ Ewing, M., and Ewing, J., *Bull. Geol. Soc. Amer.*, **70**, 303 (1959).

⁸ Fahlquist, D. A., and Hersey, J. B., *Bull. Inst. Ocean. Monaco* (in the press).

⁹ Maskaleo, V. N., *Proc. Acad. Sci. USSR Geol. Ser.*, **6**, 49 (1967).

¹⁰ Vogt, P. R., and Higgs, R. H., *Earth Planet. Sci. Lett.*, **65**, 439 (1969).

¹¹ Carey, S. W., in *A Symposium on Continental Drift* (Univ. of Tasmania, 1958).

¹² Argand, E., *Congr. Geol. Intern.*, **13**, CR., 357 (1922).

¹³ Segre, A. G., and Stocchino, C., *Inst. Idrog. d. Marina, Pub.*, F.E., 1037 (1969).

¹⁴ Segre, A. G., *Geol. Rdsch.*, **47**, 195 (1958).

¹⁵ Maccarrone, E., *Boll. Soc. Geol. Ital.*, **89**, 159 (1970).

¹⁶ Ryan, W. B. F., Workum, F., and Hersey, J. B., *Bull. Geol. Soc. Amer.*, **76**, 1261 (1965).

¹⁷ Hersey, J. B., in *Submarine Geology and Geophysics*, 75 (Butterworths, 1965).

¹⁸ Ryan, W. B. F., thesis, Columbia University (1970).

¹⁹ Heezen, B. C., and Sheridan, R., *Science*, **154**, 1644 (1966).

²⁰ Fischer, A. G., Heezen, B. C., Boyce, R. E., Bukry, D., Douglas, R. G., Garrison, R. E., Kling, S. A., Krashennnikov, V., Lisitzin, A. P., and Pimm, A. C., *Science*, **168**, 1210 (1970).

²¹ Fox, P. F., Ruddiman, W. F., Ryan, W. B. F., and Heezen, B. C., *Tectonophys.* (in the press).

Late Quaternary Meteorological and Oceanographic Developments in the Equatorial Pacific

THE statement by van Andel *et al.*¹, that the history of the late Quaternary climate at low latitudes is a controversial issue, is still valid and equatorial Pacific records show considerable variability of conditions in the atmospheric and oceanic tropospheres². The relationships of the present equatorial variability with atmospheric pressure shifts associated with the southern oscillation (SO)² can be considered together with information about the operation of the SO and geological evidence, and have led to an understanding of the meteorological and oceanographic changes which occurred in the equatorial Pacific during the late Quaternary and of their evolution.

The Pacific equatorial dry zone is a tongue shaped feature which extends westward from South America to about 180° longitude and is accompanied by relatively low temperature surface water caused by upwelling in the equatorial zone of oceanic divergence². During the past century, this zone has ranged aperiodically from a weak development over the eastern equatorial Pacific to a well developed tongue which in one case (late 1915–early 1918) extended nearly across the Pacific. (The dry condition extended westward past Kapingamarangi Atoll (1° 04' N, 154° 45' E), where a severe drought was reported³ from 1916 to 1918.) Examples of abnormally heavy precipitation over the central and western equatorial Pacific were found to be related to pressure shifts of the SO, as recorded at Darwin, Australia². Even the magnitude of pressure shifts (reflected as above normal mid-year rises) seemed to be related to the extent of abnormally heavy precipitation. Further studies indicated similar relationships between the opposite phase of the SO (below normal mid-year pressure rise at Darwin) and extensive dry zone development.

During interglacial periods in the late Quaternary, when sea levels were similar to those of today, atmospheric and oceanic circulations and interactions should also bear a close resemblance. The findings of Arrhenius⁴, which were based on a study of eastern tropical Pacific cores, indicated that the Pacific equatorial zone of divergence and upwelling was in existence throughout the Quaternary and contributed to increased biological productivity. Key features of the tropical and subtropical Pacific (that is, subtropical high pressure cells and equatorial low pressure belt between them) were thus apparently evident during the whole of the Quaternary. Arrhenius's palaeotemperature data for the surface layer of the ocean point to a steepening of the temperature gradient in outward directions from the lower temperature equatorial upwelling zone during glacial stages, and his sedimentary data show an increase in planktonic biological productivity; both findings suggest an increased rate of upwelling along the equator during glacial stages. Arrhenius⁵ believes that this intensified vertical circulation was caused by increased tropical atmospheric circulation (the trades). Hutchinson^{6,7} mentions phosphate deposits under tropical forests on the Purdy Islands (2° 55' S, 146° 25' E) and also millions of tons of phosphate rock on Nauru (0° 32' S, 166° 55' E) and Ocean (0° 52' S, 169° 35' E) Islands. These islands now lack the large bird colonies and persistent dry conditions necessary to develop and preserve large guano accumulations, but if tropical circulation was stronger and equatorial upwelling more pronounced during glacial stages, extensive, nutrient rich upwelled waters would have caused highly increased biological productivity in this region. Increased production of phytoplankton, and therefore of zooplankton and smaller fishes, would have provided support for large island bird colonies and thus the development of large guano deposits. The persistent equatorial dry zone, with its cool upwelled surface waters, would favour accumulation of guano by preventing deposits from being washed away by heavy tropical rains. Hutchinson⁷ could not at first decide whether glacials or interglacials were responsible

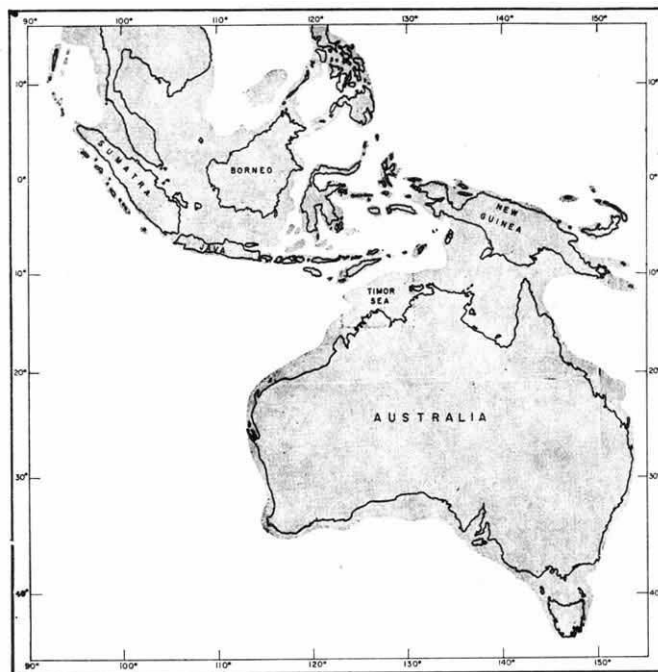


Fig. 1 Distribution of land and sea in the Indonesia-Australia region during the last Pleistocene glaciation (Wisconsin II); sea level at -120 m (according to van Andel *et al.*¹ and Curry^{12,13}).

for the extraordinary phosphatization of the Pleistocene. He now feels that Arrhenius's results clearly identify glacial stages as times of maximum phosphatization. Geological evidence thus favours the extension of a persistent, well developed dry zone across the Pacific during glacial stages. In view of the existing variable dry zone, the problem is to find out what physical changes caused the equatorial, meteorological and oceanographic conditions of glacial stages.

We must consider the mode of operation of the SO and its role in dry zone development in order to solve the problem. The term southern oscillation was introduced by Sir Gilbert Walker⁸, and is a fluctuation in the intensity of the intertropical general atmospheric and oceanic circulation over the Indo-Pacific region⁹. If atmospheric pressure is abnormally low in the Malay-Indonesia area, it is unusually high in the subtropical south-east Pacific¹⁰, and the large pressure gradient between the subtropical high and Indonesia low strengthens the associated atmospheric circulation. Oceanic circulation is therefore accelerated, and the Peru current and upwelling along the South American west coast show increases of intensity which are accompanied by lower surface water temperatures. The south equatorial current is accelerated and equatorial upwelling is more intense, causing lower sea surface temperatures and an extensive, well developed dry zone. It follows¹⁰ that surface and near surface waters arriving in the Malay-Indonesia area from the east are cooler than normal and cause a rise in atmospheric pressure. If air pressure is above normal in the Malay-Indonesia area, it is below normal in the subtropical south-east Pacific and the low pressure gradient between the subtropical high and equatorial low causes a slackening in atmospheric circulation and a deceleration in oceanic circulation¹⁰. The Peru Current becomes weaker, coastal upwelling slackens and associated surface waters become warmer. The south equatorial current is decelerated, equatorial upwelling slackens, sea surface temperatures rise and the dry zone becomes less extensive and poorly defined. At such times, precipitation becomes abnormally heavy over the western and central parts of the equatorial Pacific and very heavy rain and the disastrous El Niño often appear earlier along and seaward of the tropical west coast of South America during the southern hemisphere summer and, sometimes, autumn². The cycle is completed because surface

waters arriving in the Malay-Indonesia area are warmer than normal and cause a decrease in atmospheric pressure¹⁰.

Troup¹¹ considers exchange of air between eastern and western hemispheres in the vertical dimension and links it up with variations in a mean toroidal circulation driven by temperature differences between the two core areas. In the interests of simplicity, he considers that there is a single drift of primary importance in the upper troposphere from 500 to 200 millibars, and that this flows from the negative area (where the warm surface low pressure centre is located) across the Pacific to its central and eastern regions. It is compensated by return flow near the surface from the eastern Pacific to the negative area¹¹. This circulation descends over the central and eastern Pacific, and ascends over the negative area and adjacent regions. There is therefore a toroidal circulation in the vertical and zonal plane. Pressure changes which result in SO index variations are caused by variations in this circulation.

The persistent equatorial upwelling during glacial stages and the associated dry zone which extended across the Pacific seem to have been caused by the lowering of the sea level. The shallow sea areas in the Malay-Indonesia area and between New Guinea and Australia (Fig. 1) emerged as the sea level dropped. This prevented cooler waters, associated with stronger south-east trades and equatorial upwelling (high index phase of SO), from entering the Malay-Indonesia area. It eliminated the mechanism which controls atmospheric and oceanic fluctuations of the SO, and caused the SO to be arrested in its high index phase. The well developed Indonesian equatorial low and South Pacific subtropical high therefore persisted and the strong tropical circulation (trades) and intensified equatorial upwelling evolved. This situation persisted until the sea level rose sufficiently during an interglacial to allow redevelopment of the SO.

I thank the US National Science Foundation for financial support and Dr Tj. H. van Andel for encouragement and helpful comments. I also thank Dr Wayne V. Burt and Dr T. C. More for help with the manuscript.

W. H. QUINN

Department of Oceanography,
Oregon State University,
Corvallis, Oregon

Received July 28; revised September 28, 1970.

- ¹ van Andel, Tj. H., Heath, G. R., Moore, T. C., and McGeary, D. F. R., *Amer. J. Sci.*, **265**, 737 (1967).
- ² Quinn, W. H., and Burt, W. V., *J. Appl. Meteorol.*, **9**, 20 (1970).
- ³ Wiens, H. J., *Atoll Research Bull.*, No. 48 (National Academy of Sciences, Washington, 1956).
- ⁴ Arrhenius, G., *Rep. Swedish Deep Sea Expedition*, **5** (1952).
- ⁵ Arrhenius, G., in *Rosby Memorial Volume* (edit. by Bolin, B.), 121 (Rockefeller Institute Press, New York, 1959).
- ⁶ Hutchinson, G. E., *Bull. Amer. Mus. Nat. Hist.*, **96** (1950).
- ⁷ Hutchinson, G. E., in *Biology of Phosphorus* (edit. by Wolterink, L. F.), 1 (Michigan State College Press, 1952).
- ⁸ Walker, G. T., *Mem. Indian Meteorol. Dep.*, **24**, 275 (1924).
- ⁹ Berlage, H. P., *Meded. Verh. (K. Ned. Meteorol. Inst., No. 88)* (1966).
- ¹⁰ Berlage, H. P., *Ann. New York Acad. Sci.*, **95**, 490 (1961).
- ¹¹ Troup, A. J., *Quart. J. Roy. Meteorol. Soc.*, **91**, 490 (1965).
- ¹² Curry, J. R., *Geol. Soc. Amer. Bull.*, **72**, 1707 (1961).
- ¹³ Curry, J. R., in *The Quaternary of the United States* (edit. by Wright, H. E., and Frey, D. G.), 723 (Princeton University Press, 1965).

Evidence for Crust in the Deep Ocean derived from Continental Crust

FIG. 1 shows the profile of a free-air gravity anomaly obtained by HMS Hecate in the Bay of Biscay in 1967 (with two gravimeters back-to-back to eliminate cross-coupling error). The track is shown in Fig. 2 together with the available deep-water refraction stations; D12 was shot by Ewing and Ewing¹ and

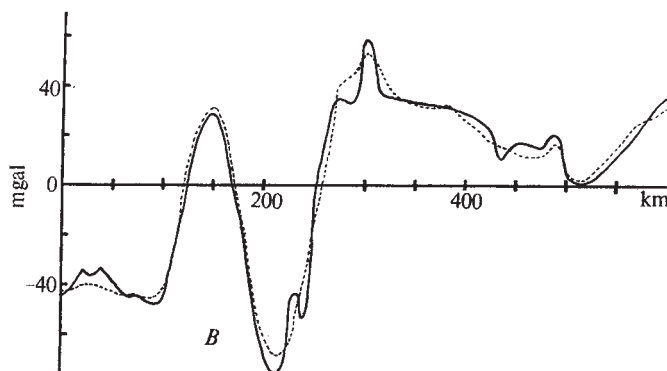


Fig. 1 Observed (—) and calculated (---) free-air gravity anomalies.

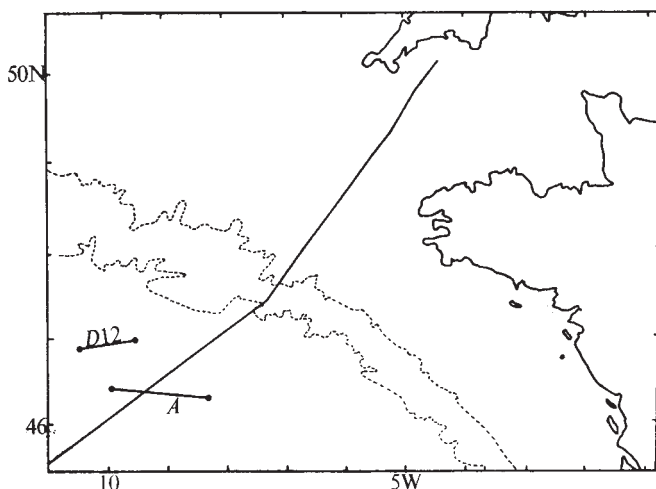


Fig. 2 Track chart. 100 and 2,000 fathom contours shown dotted.

A by RRS Discovery in 1968 (R. B. Whitmarsh, personal communication).

A two-dimensional model (Fig. 3) was calculated to fit the observed gravity taking into account these seismic data and those of Day on the shelf². No attempt has been made to fit the observations to better than a few mGal, and seismic velocities have been rather arbitrarily grouped together and associated with densities according to the relationship described by Talwani³. The main continental block has been assumed to end under the 2,000 m isobath as suggested by Worzel⁴; the depth of about 30 km to Moho under the continent is in fair agreement with the results of Bunce *et al.*⁵ and of Agger and Carpenter⁶.

The most striking feature of the model is the very pronounced basement ridge at B. The gravity map of the Bay of Biscay⁷ shows that this profile is a crossing of a gravity ridge in front of the Meriadzek Terrace. The observed magnetic anomaly along this profile is shown in Fig. 4, taken from the magnetic map of the Bay⁸. For comparison, Fig. 4 also shows the anomaly expected from the basement topography in a two-dimensional model if all the basement down to 10 km had a magnetization in the direction of the Earth's present field of -300 gamma. Although a magnetic anomaly is observed along the profile, it is much more diffuse than the basement

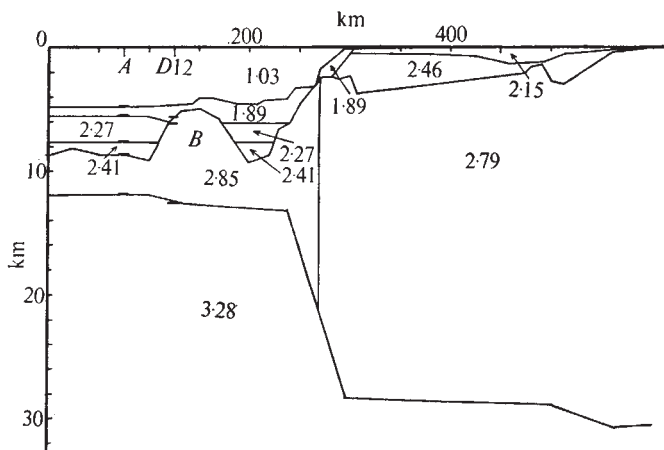


Fig. 3 Model of structure. Figures are densities in g/cm^3 . Short solid lines show structure under refraction stations.

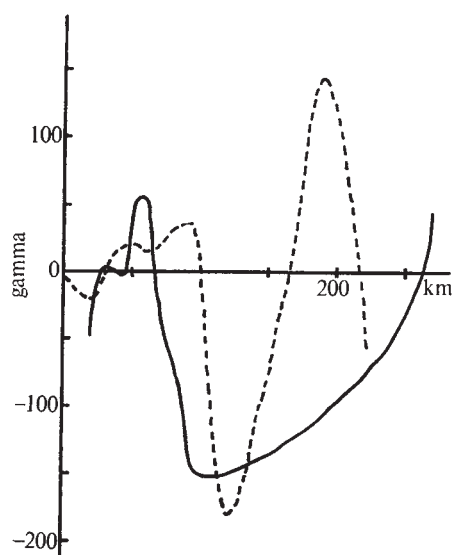


Fig. 4 Observed (—) and calculated (---) magnetic anomalies.

topography would suggest. We conclude that the ridge is essentially non-magnetic.

Furthermore, the main crustal layer at Station D12, which is partially on the line of the ridge, has a velocity of 6.14 km s^{-1} which is lower than the more "oceanic" velocity of 6.47 km s^{-1} at station A and near to the mean velocity of the continental metamorphic basement as given in ref. 2.

It is difficult to think of this non-magnetic, rather low-velocity ridge as being other than continental in origin. If this is so, its presence in 1,500 fathoms of water implies a down-faulting process at the continental margin as first suggested by Day⁹ and recently advocated by Cholet *et al.*¹⁰. This must have been accompanied by considerable crustal thinning. The magnetic evidence shows that the entire region at the foot of the Brittany continental slope in Biscay is as free from short-wavelength magnetic anomalies as the present section, so it is very possible that this whole region is downfaulted thinned continental crust.

M. BACON
F. GRAY

Department of Geodesy and Geophysics,
University of Cambridge

Received September 7, 1970.

¹ Ewing, J., and Ewing, M., *Bull. Geol. Soc. Amer.*, **70**, 291 (1959).

² Day, A. A., Hill, M. N., Laughton, A. S., and Swallow, J. C., *Quart. J. Geol. Soc. Lond.*, **122**, 15 (1956).

- ³ Talwani, M., Sutton, G. H., and Worzel, J. L., *J. Geophys. Res.*, **64**, 1545 (1959).
⁴ Worzel, J. L., *Geology of Shelf Seas* (edit. by Donovan, D. T.) (Oliver and Boyd, London, 1968).
⁵ Bunce, E. T., Crampin, S., Hersey, J. B., and Hill, M. N., *J. Geophys. Res.*, **69**, 3853 (1964).
⁶ Agger, H. E., and Carpenter, E. W., *Geophys. J. Roy. Astr. Soc.*, **9**, 69 (1964).
⁷ Bacon, M., Gray, F., and Matthews, D. H., *Earth Planet. Sci. Lett.*, **6**, 377 (1969).
⁸ Matthews, D. H., and Williams, C. A., *Earth Planet. Sci. Lett.*, **4**, 315 (1968).
⁹ Day, A. A., *Deep Sea Res.*, **5**, 249 (1959).
¹⁰ Cholet, J., Danotte, B., Grau, G., Debyser, J., and Montadert, L., *Rev. Inst. Franc. Petrole*, **23**, 1029 (1968).

Energy Levels and Lorentz Invariance

THE relativistic soundness of the quantum theoretical formula

$$h\nu = E' - E \quad (1)$$

has been questioned by Sygne¹. In an interesting note, he derives instead the formula

$$h\nu = (m'^2 - m^2)c^2/2m' \quad (2)$$

where m' is the relativistic mass of the system (atom) in its initial state S' in the initial rest frame (the centre of mass frame) and m is the lower energy state S of the system (mc^2 being the proper energy in this state). The energies E' and E are measured in the initial and final rest frame of the system. We do not in any way disagree with Sygne, but wish to give a slightly different formulation of this question which, in a sense, preserves (1) by giving it an interpretation fully consistent with equation (2). This requires all the energies in equation (1) to be measured in the same frame.

A system A of proper energy E_{AO} is at rest in an inertial frame I and decays into two part systems B_1, B_2 whose momenta and energies in I are p_1, p_2, E_1, E_2 . Then if $E_A = E_{AO}$, and $p_A = p_{AO} = 0$ in I

$$E_1 + E_2 = E_{AO} \quad (3)$$

$$p_1 + p_2 = 0 \quad (4)$$

$$E_i^2 - p_i^2 c^2 = E_{i0}^2 \quad (i = A, 1, 2) \quad (5)$$

If the momenta are eliminated, we find that

$$E_1 = \frac{E_{10}^2 - E_{20}^2 + E_{AO}^2}{2E_{AO}} \quad (6)$$

$$E_2 = \frac{E_{20}^2 - E_{10}^2 + E_{AO}^2}{2E_{AO}} \quad (7)$$

Thus if B_1 is the principal fragment, A can be imagined to "emit" B_2 and the energy in I of the emitted fragment is (3 and 6)

$$E_2 = E_{AO} - E_1 = \frac{E_{20}^2 - E_{10}^2 + E_{AO}^2}{2E_{AO}} \quad (8)$$

The energy $E_{20} = 0$ for photon emission at frequency ν in frame I and equation (8) yields

$$h\nu = E_{AO} - E_1 = \frac{E_{AO}^2 - E_{10}^2}{2E_{AO}} = (E_{AO} - E_{10}) \frac{E_{AO} + E_{10}}{2E_{AO}} \quad (9)$$

Equations (1) and (2) are both valid provided E' and E are interpreted as system energies before and after emission, both measured in the centre of mass frame ($E_{AO} \rightarrow E' = m'c^2$, $E_1 \rightarrow E$, $E_{10} \rightarrow mc^2$).

The result (equation (9)) can, however, be developed in a different way. If D is some invariant quantity, for example, the sum Mc^2 of all the proper masses constituting the system, excess energies E' and E can be introduced in the centre of mass frame I by writing

$$E_{AO} \equiv m'c^2 \equiv D + E' \quad (10)$$

$$E_1 \equiv D + E \quad (11)$$

If $E_{10} \equiv mc^2$, equation (9) becomes

$$h\nu = E' - E = (m'^2 - m^2) c^2 / 2m'$$

In other words, both equations (1) and (2) are valid provided the part E of the system energy is interpreted after emission as an energy measured in the centre of mass frame.

If, on the other hand, the part E of the system energy after emission was interpreted as being measured in the proper frame of the system after emission, equation (10) remains valid but equation (11) is replaced by

$$E_{10} = D + E_0 \quad (12)$$

A slightly different frequency, ν_0 , then emerges

$$h\nu_0 \equiv E_{AO} - E_{10} = E' - E_0 \quad (13)$$

This is the form of equation (1) used by Synge. Equations (9) and (13) can be used to relate ν_0 to ν

$$\frac{\nu_0 - \nu}{\nu_0} = \frac{E_{AO} - E_{10}}{2E_{AO}} = \frac{h\nu_0}{2E_{AO}} \equiv K \quad (14)$$

The quantity (k) was calculated by Synge as $\sim 10^{-9}$, and it measures the error made in using equations (10) and (12) for the interpretation of the energies which are seen in equation (1). This error, that is, the neglect of recoil, arises from the use of two distinct inertial frames for the energies on the right side of equations (1) or (13)—the rest frames before and after emission. If, instead, equations (10) and (11) are used, no error is made in using equation (1).

The recoil error, equation (14), incurred by using ν_0 instead of ν can be calculated already non-relativistically to within $O(K^3)$, provided that only the photon is represented as a classical particle whose energy ($h\nu_1$, say) is c times its momentum. This is illustrated by one of the consequences of energy and momentum conservation

$$h\nu_1 = E_{AO} - \left[E_{10} + \left(\frac{h\nu_1}{c} \right)^2 \frac{2E_{10}}{c^2} \right] \quad (15)$$

If the quadratic equation is solved for ν_1 , one finds from equation (13) that

$$\begin{aligned} \frac{\nu_0 - \nu_1}{\nu_0} &= \frac{1}{2} \frac{h\nu_0}{E_{10}} - \frac{1}{2} \left(\frac{h\nu_0}{E_{10}} \right)^2 + \frac{5}{8} \left(\frac{h\nu_0}{E_{10}} \right)^3 + \dots \\ &= K + K^3 + \dots \end{aligned} \quad (16)$$

and

$$\frac{\nu - \nu_1}{\nu} = K^3 + \dots \sim 10^{-27} \quad (17)$$

Thus although it is important to consider recoil, equation (17) shows that it is less important to treat it relativistically.

P. T. LANDSBERG
J. L. HINDMARSH

Department of Applied Mathematics and
Mathematical Physics,
University College,
Cardiff

Received October 27, 1970.

¹ Synge, J. L., *Nature*, **228**, 271 (1970).

Rotation of the Variation of Upper Atmosphere

FROM observations of satellite orbits it has been deduced that the atmosphere above about 200 km altitude rotates 20–30% faster than the Earth, so that there exists a net west-to-east wind of order 100 m s^{-1} (refs. 1, 2). This “super-rotation” has not yet been satisfactorily explained. The wind systems driven by the diurnal heating and cooling of the thermosphere³ do not produce any significant net rotation at mid-latitudes⁴. The satellite data are somewhat weighted towards low latitudes so the rotation may be most pronounced there; calculations suggest that the thermospheric winds may produce some net rotation at low latitudes⁵, though probably not enough to account fully for the observations. Ionospheric motions driven by dynamo electric fields in the E region do not seem to make any significant difference to this result⁵.

I have examined a possible cause of eastward rotation of the equatorial atmosphere. It is suggested that at night an electric polarization field is developed in the ionospheric F region by the action of an eastward neutral air wind (velocity U). The polarization field causes the F region plasma to drift with velocity V in the direction of the wind, thus reducing the frictional “ion-drag” force, proportional to $(U-V)$, that opposes the air motion. Ion-drag in fact provides the principal limitation on wind speeds at F layer heights (around 300 km); the Coriolis force resulting from the Earth’s rotation vanishes at the geographic equator, while viscosity—though important at great heights—does not have any great effect on wind speed at around 300 km⁶. Viscous forces come into play to limit the wind speed if ion-drag is greatly reduced, and should be taken into account in any future calculations.

The polarization field develops because a neutral air wind U blowing perpendicular to the geomagnetic field lines produces an ion drift, normal to both the wind and the magnetic field, with speed Uv/ω (where ω =ion gyrofrequency, v =collision frequency of ions with neutral particles). At 300 km altitude $v/\omega \sim 0.003$ so that a wind of 100 m s^{-1} produces an ion drift of 0.3 m s^{-1} . For the electrons the ratio v/ω is so much smaller than for ions that the wind produces negligible drift across the magnetic field. Thus the wind tends to drive an electric current, proportional to $N_F U v / \omega$ where N_F is the ion (or electron) concentration: this may be termed the “F layer dynamo current”.

Although the F layer dynamo operates at all latitudes, its effects are of particular interest in the equatorial F layer where the ion drift is vertical, and therefore produces vertical charge separation. The resulting electric field tends to drive an electric current along the highly conducting geomagnetic field lines and through the E layer (Fig. 1). Thus the E layer in subtropical latitudes, magnetically linked to the equatorial F layer, tends to short-circuit the equatorial F layer dynamo.

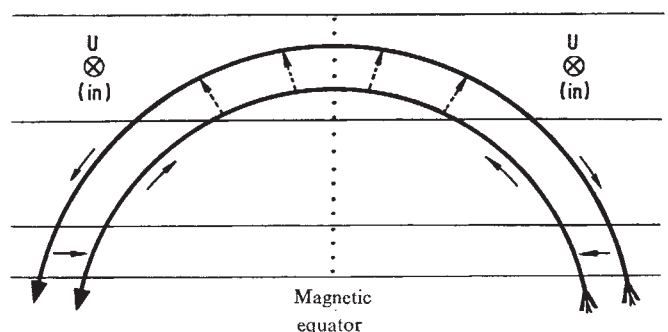


Fig. 1 View eastward in the equatorial ionosphere. The curved geomagnetic field lines passing through the equatorial F layer intersect the E layer about 10° N and S of the equator. A wind U blowing eastward (into the plane of the diagram) causes ions to drift across the field lines with speed Uv/ω (broken arrows). If the E layer is sufficiently conducting, electric currents flow in closed circuits as shown by arrows.

Whether the short-circuiting is effective depends on the E layer conductivity, proportional to the E layer ion concentration N_E , and on geometrical factors. If N_E is so large that the short-circuiting is very effective, the wind U produces no ion motion so that $V=0$. But if N_E is very small the E layer is non-conducting; a polarization field builds up until the ions and electrons drift eastward with speed $V=U$, and then no further charge separation occurs. Detailed calculations (to be described elsewhere) suggest that in the equatorial ionosphere the degree of short-circuiting is such that $V/U \approx 0.2$ by day; at night $V/U \approx 0.8$ and in this case the ion-drag is reduced to about 20% of the value it would have in the absence of polarization fields. This considerably increases the wind speed at night when the wind is predominantly eastward so that $\bar{U}$, the average of U over 24 h, is eastward. Because the air density ρ varies diurnally at 300 km, the eastward momentum transport is better described by the "weighted" average $(\rho\bar{U})/\bar{\rho}$.

The local-time variation $U(t)$ of eastward wind velocity at 300 km altitude has been computed by integrating a simplified equation of motion which includes inertia, the acceleration due to east-west gradients of air pressure, and ion-drag:

$$dU/dt = P - KN_F (U - V) \quad (1)$$

The acceleration P is computed from the mean of the "summer" and "winter" diurnal temperature variations at Jicamarca, near the magnetic equator (Fig. 6 of ref. 7), the relation between pressure, density and temperature at 300 km altitude being taken from ref. 8. In the ion-drag term the constant $K = 7.3 \times 10^{-16} \text{ m}^3 \text{ s}^{-1}$; values of peak electron concentration $NmF2$ recorded at Huancayo, September 1967, are used for N_F . Three cases are illustrated in Fig. 2.

This analysis suggests that F layer winds and the associated polarization fields cause at least some super-rotation at low latitudes. If they do, the F layer ions and electrons would

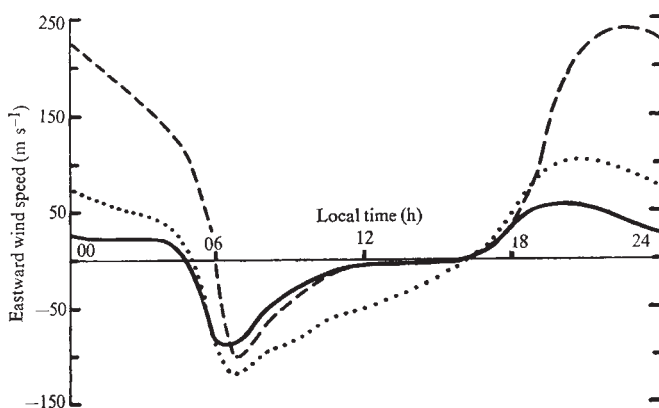


Fig. 2 Computed local-time variation of eastward wind speed at 300 km altitude at the equator. —, Polarization neglected so that $V=0$. Then $\bar{U}=3 \text{ m s}^{-1}$ which is insignificant. ---, F layer polarization included, the ratio V/U being computed separately from reasonable values of E and F layer parameters. $\bar{U}$ depends on the night-time value of N_E which is not very accurately known. If $N_E = 5 \times 10^9 \text{ m}^{-3}$ at night (as used for Fig. 2), $\bar{U} = 74 \text{ m s}^{-1}$ which corresponds to a super-rotation of 15%; the "weighted" average $(\rho\bar{U})/\bar{\rho} = 57 \text{ m s}^{-1}$. If instead $N_E = 3 \times 10^9 \text{ m}^{-3}$ at night then $\bar{U} = 107 \text{ m s}^{-1}$ (22% super-rotation) and $(\rho\bar{U})/\bar{\rho} = 81 \text{ m s}^{-1}$, F layer polarization neglected, but instead the effect of E layer dynamo fields is studied by imposing an ion drift velocity V with an appropriate phase⁹ (time t in h):

$$V = 50 \cos \left\{ \frac{\pi}{12} (t+2) \right\} \text{ m s}^{-1} \quad (2)$$

In this case $\bar{U} = 5 \text{ m s}^{-1}$ only so that the E layer dynamo field produces no appreciable super-rotation. This suggests that if E layer and F layer fields are combined the value of $\bar{U}$ would be much the same as that caused by the F layer effects alone.

also drift eastward at night, though not at quite the same speed as the air. In fact eastward drifts of order 100 m s^{-1} are observed in low latitudes at night¹⁰.

I thank Professor P. C. Kendall and Drs E. N. Bramley and R. J. Moffett for stimulating discussion.

H. RISHBETH

Radio and Space Research Station,
Slough,
Buckinghamshire

Received July 31, 1970.

- ¹ King-Hele, D. G., *Planet. Space Sci.*, **12**, 835 (1964).
- ² King-Hele, D. G., *Nature*, **226**, 439 (1970).
- ³ King, J. W., and Kohl, H., *Nature*, **206**, 699 (1965).
- ⁴ Bailey, G. J., Moffett, R. J., and Rishbeth, H., *J. Atmos. Terr. Phys.*, **31**, 253 (1969).
- ⁵ Challinor, R. A., *Planet. Space Sci.*, **17**, 1097 (1969).
- ⁶ Geisler, J. E., *J. Atmos. Terr. Phys.*, **28**, 703 (1966).
- ⁷ Waldeufel, P., and McClure, J. P., *Ann. Geophys.*, **25**, 785 (1969).
- ⁸ Jacchia, L. G., *Smithsonian Contrib. Astrophys.*, **8**, 215 (1965).
- ⁹ Maeda, H., *Proc. Intern. Conf. Ionosphere*, Inst. of Phys. and Phys. Soc., London, 187 (1963).
- ¹⁰ Kent, G. S., and Wright, R. W. H., *J. Atmos. Terr. Phys.*, **30**, 657 (1968).

Clean Air Act

I SHOULD like to extend Brazell's recent discussion of the meteorological consequences of the Clean Air Act of 1956 which was confined chiefly to visibility and sunshine¹. I shall provide further direct and indirect evidence concerning other meteorological variables such as atmospheric stability, solar radiation, illumination and air temperature, and the diverse interactions between meteorological elements and air pollution.

Because meteorological variables are related to each other and to air pollution in a complex manner, the evidence should be assessed by indirect treatment of the data where possible. Trends in urban smoke pollution, and even urban changes relative to those in surrounding areas, do not provide complete proof of the efficiency of the procedures resulting from the Clean Air Act because of the effects of secular, periodic and shorter term climatic changes.

One of the strongest indications of the effect of the Act was the absence of the usual cyclic pattern of winter smoke concentration at Kew Observatory after 1956 (ref. 2). In the 10 yr cycles of smoke pollution, peaks occur when the combined effect of low wind speed, great atmospheric stability and low air temperature attains a maximum. There is no apparent reason to suppose that this cycle of meteorological events has suddenly ceased, especially because there has been a peak in sulphur dioxide air pollution—a form of pollution which has not been affected to the same degree by government legislation. The absence of a smoke peak is thus highly significant.

Clearly the meteorological trends indicated by the cyclic pattern of smoke pollution (with a peak around 1962) could, irrespective of legislation, include a general improvement of visibility from 1962 to 1967, particularly in towns and rural areas affected by smoke. Therefore the improvement of visibility described by Dinsdale³ cannot be used justifiably as direct evidence of an improvement resulting from the Clean Air Act.

Similarly, the causes of an increased duration of "bright" sunshine or a percentage increase in sunshine or even an urban increase relative to surrounding rural areas are difficult to assess because, for example, a general trend to drier and windier conditions could lead to a tendency to increased and equal amounts of sunshine in urban and rural areas, that is, to a greater relative increase of sunshine in urban areas. Some of the difficulties of assessment may be resolved by detailed reference to changes in other meteorological variables⁴, but

also, and more easily, by the use of direct solar radiation data rather than sunshine data.

Mean monthly maximum hourly values of direct solar radiation at normal incidence at Kew Observatory show that in each of the months from April to September inclusive, there was a decrease from the decade 1948–57 to the decade 1958–67, in accordance with the more general global trend described by Pivovarova⁵, but in December and January this trend seems to have been reversed. Indeed, the calendar month differences, expressed as percentages of the monthly averages, form an approximate sine wave and when this curve (with one harmonic and two degrees of freedom) is taken into consideration, a variance analysis shows that the significance of the pattern of decadal differences is less than 0.01.

With reference to these changes in solar radiation, changes in surface humidity do not suggest any marked trends in atmospheric transmissivity due to trends in atmospheric water content. It is noticeable that a proportion of radiation maxima occurred after “washing out” by rain or showers, but maxima often occurred with persistent sunny anticyclonic weather.

Another interesting change from the 1950s to the 1960s was a relative increase in central London of winter illumination (expressed as a percentage of that obtained at Kew Observatory) from 0.8 to generally 0.9 to 1.0 (ref. 6).

Long term changes of air temperature in central London relative to surrounding rural areas⁶ do not at first seem to be consistent with the thesis that the Clean Air Act has led to a decrease of urban smoke pollution. Reduction of smoke could be expected to cause relatively increased daily maximum temperatures and decreased daily minimum temperatures. In the London area, between the 1930s and about 1950—a period of social progress and then fuel rationing—such changes were observed but a “levelling-out” followed. A continued relative decrease of minimum air temperatures in London after 1950 may have been checked by increased fuel consumption and artificial atmospheric heating: a relative increase of maximum temperatures may have ceased as a result of natural climatic changes, such as increased wind speed.

In general, meteorological data show that as a consequence of the Clean Air Act there are smaller concentrations of smoke pollution than would have occurred otherwise, but the quantitative assessment of that part of the improvement which can be attributed directly to the Clean Air Act would require much further analysis.

E. N. LAWRENCE

*Meteorological Office,
Bracknell, Berkshire*

Received September 7, 1970.

¹ Brazell, J. H., *Nature*, **226**, 694 (1970).

² Lawrence, E. N., *Weather*, **21**, 367 (1966).

³ Dinsdale, F. E., *Meteorol. Mag.*, **97**, 314 (1968).

⁴ Lawrence, E. N., *Weather* (in the press).

⁵ Pivovarova, Z. I., *Glav. Geof. Obs., Tr. Vyp.*, **233**, 17 (Leningrad, 1968).

⁶ Lawrence, E. N., *Meteorol. Mag.*, **98**, 1 (1969).

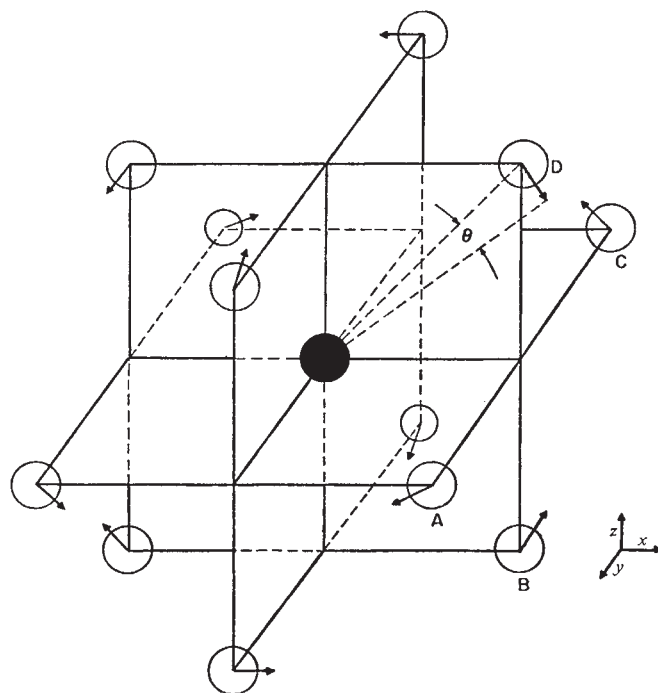


Fig. 1 The distortions of a 13 atom cluster. The central atom is a solid circle, and its 12 nearest neighbours are open circles shown lying in the xy , yz and zx planes. Each atom rotates by an angle θ in the directions indicated.

We assume that the atoms interact by a pair-wise additive Lennard-Jones potential of the form

$$V(r) = 4e \left\{ \left(\frac{r_0}{r} \right)^{12} - \left(\frac{r_0}{r} \right)^6 \right\} \quad (1)$$

already used to study rare gas solids⁸. The exact numerical results presented here will depend on the potential form but the qualitative results will not.

A spherical cluster of atoms can be built up in a cubic configuration in the following way: first, a central atom is located at (0, 0, 0); then its 12 next nearest neighbours are added at the 12 positions having coordinates of the form $a/\sqrt{2}(1, 1, 0)$; the 6 second nearest neighbours are added at $a/\sqrt{2}(2, 0, 0)$; the 24 third nearest at $a/\sqrt{2}(2, 1, 1)$; the 12 fourth nearest at $a/\sqrt{2}(2, 2, 0)$; and so on. Thus we can build spherical clusters of atoms containing 1, 13, 19, 43, 55, ...

We wish to find the minimum energy configuration of a spherical cluster of n atoms by allowing the original cubic structure to relax so as to minimize the energy expressed as a sum of Lennard-Jones potentials. This has been done exactly for $n \leq 87$ by minimizing the energy along the normal vibrational coordinates.

Under this procedure, clusters of 19, 43, 79 and 87 retain their basic cubic symmetry, but the 13 and 55 atom clusters distort significantly. The 13 atom distortion is shown in Fig. 1, in which the nearest neighbour distances AB, BC, CD and DA are slightly increased (see ref. 9). The pseudorotation pictured in Fig. 1 is also accompanied by a small change in the distance from the central atom to its next nearest neighbour.

Table 1 gives the coordinates of the undistorted 13 atom cluster and those in the minimum energy configuration. The energy of the distorted structure is 7% less than that of the cubic structure, chiefly because of the increase in the number of next nearest neighbour bonds (Table 2). It is not possible to define precisely the volume of such a small cluster, but this must be proportional to the cube of the distance from the central atom to an atom in the outermost shell so that, from Table 1, the volume of the distorted structure is 2% less and its density 2% greater than that of the normal cubic close packed structure.

Densely Packed Small Clusters of Atoms

WHEN real materials are randomly packed, the possible existence of local very dense regions may affect the porosity of the system. Earlier packing studies have dealt with hard spheres^{1–7}, but we now examine the packing of real atoms—particles with a potential having a long range attraction and a short range repulsion. Real potentials allow a distribution of nearest, neighbour distances. We show, for a Lennard-Jones potential, that there exist very dense low energy structures for clusters of 13 and 55 atoms.

BIOLOGICAL SCIENCES

Table 1 Undistorted 13 Atom Cluster

Cubic close packed	Distorted
(0, 0, 0)	(0, 0, 0)
{(1, 1, 0)}	{(0.741, 1.193, 0)}
{(1, 0, 1)}	{(1.193, 0, 0.741)}
{(0, 1, 1)}	{(0, 0.741, 1.193)}

The coordinates of a 13 atom cluster in an undistorted cubic close packed configuration and in the distorted configuration. $\{(i, j, k)\}$ refers to the set of coordinates $a\sqrt{2}(\pm i, \pm j, \pm k)$ where $a/\sqrt{2}$ is the bulk nearest neighbour distance.

Table 2 Bond Length Distribution in a 13 Atom Cluster

Bond length	Cubic close packed	Distorted
0.995	0	12
1.000	36	0
1.045	0	30
> 1.35	42	36

The normal nearest neighbour distance is taken as 1.0.

The 55 atom cluster undergoes a distortion of the same symmetry as shown in Fig. 1 for 13 atoms, and the physical origin of this distortion is similar. The coordinates are given in Table 3, and the energy of the distorted cluster is 4% less than that of the normal cubic close packed cluster. The density of the distorted cluster is 6% greater than that of the normal cluster.

Table 3 Undistorted 55 Atom Cluster

Cubic close packed	Distorted
(0, 0, 0)	(0, 0, 0)
{(1, 1, 0)}	{(0.718, 1.159, 0)}
{(1, 0, 1)}	{(1.159, 0, 0.718)}
{(0, 1, 1)}	{(0, 0.718, 1.159)}
{(2, 0, 0)}	{(2.376, 0, 0)}
{(0, 2, 0)}	{(0, 2.376, 0)}
{(0, 0, 2)}	{(0, 0, 2.376)}
{(2, 1, 1)}	{(1.927, 1.188, 0.736)}
{(1, 2, 1)}	{(0.736, 1.927, 1.188)}
{(1, 1, 2)}	{(1.188, 0.736, 1.927)}
{(2, 2, 0)}	{(1.463, 2.359, 0)}
{(2, 0, 2)}	{(2.359, 0, 1.463)}
{(0, 2, 2)}	{(0, 1.463, 2.359)}

The coordinates of a 55 atom cluster in an undistorted cubic close packed configuration and in the distorted configuration. See Table 1 for explanations.

In this brief note we have pointed out that, for real potentials, small clusters of 13 and 55 atoms can exist in very dense low energy configurations.

J. J. BURTON

Henry Krumb School of Mines,
Columbia University,
New York, NY 10027

Received August 27, 1970.

- Bernal, J. D., *Nature*, **185**, 68 (1960).
- Bernal, J. D., *Proc. Roy. Soc., A*, **280**, 299 (1964).
- Scott, G. D., *Nature*, **201**, 382 (1964).
- Wise, M. E., *Philips Res. Rep.*, **7**, 321 (1952).
- Gilbert, E. N., *Canad. J. Math.*, **16**, 286 (1964).
- Boerdijk, A. H., *Philips Res. Rep.*, **7**, 303 (1952).
- Gray, W. A., *The Packing of Solid Particles* (Chapman and Hall, London, 1968).
- Allen, R. E., and deWette, F. W., *J. Chem. Phys.*, **51**, 4820 (1969).
- Burton, J. J., *J. Chem. Phys.*, **52**, 345 (1970).

Induction of Mitochondrial DNA Synthesis by Polyoma Virus

THE infection of confluent cultures of "permissive" cells by polyoma virus promotes a sharp increase in the rate of cellular DNA synthesis¹⁻³ in the cells in which the production of virus eventually takes place⁴. It is also known from investigations carried out with viral mutants that the induction of DNA synthesis in the host cells does not require viral DNA replication^{5,6}. Nevertheless it is known from inactivation experiments that the stimulation of cellular DNA synthesis is a function of the viral genome, although the processes involved at the molecular level remain rather obscure^{4,7,8}. In systems of cells where multiplication is controlled by population density, viral infection with either polyoma or SV40 releases cells from contact inhibition. DNA synthesis does not shift to an un-

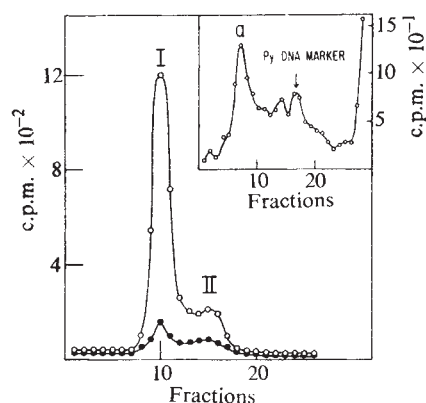


Fig. 1 Incorporation of ³H-thymidine into the mitochondrial DNA of 3T3 cells infected with wild type polyoma virus. 1×10^7 cells were infected, 24 h after they had reached confluence, with polyoma virus at a multiplicity of 200 p.f.u. cell. Twenty-five hours after infection, cells were labelled for 4 h (in conditioned medium) with 6 μ Ci/ml. of ³H-thymidine (specific activity 6 Ci/mmol). An equal number of mock-infected cells from the same batch were labelled simultaneously. Mitochondrial DNA was isolated according to a procedure already described¹². Cells were suspended in 0.6 ml. of 10 mM Tris (pH 7.6), 1 mM EDTA, 1 mM spermidine, made 0.5% in 'Nonidet P 40' and stirred for 20 s. Nuclei were sedimented at 1,000g; the cytoplasmic extracts were made 1% in sodium dodecylsulphate, layered onto 15–30% sucrose-SDS gradients¹² and centrifuged for 16 h at 25,000 r.p.m., 25° C, in the SW 25.3 Spinco rotor. Fractions were collected from the gradients by an automatically recording Gilford spectrophotometer and an aliquot from each fraction was assayed for radioactivity. The rest of the fractions corresponding to the 45–22S region were pooled and precipitated with alcohol. Nucleic acids were resuspended in 10 mM Tris (pH 7.6), 1 mM EDTA, made 2 M in CsCl and left overnight at 5° C. This modification of the previous procedure¹² causes the rRNA to precipitate (when large amounts of rRNA are present, omission of this step may result in important losses of supercoiled DNA molecules in the pellet, during the successive equilibrium-density centrifugation). The solution, cleared of precipitated RNA by centrifugation at 15,000g for 10 min, received CsCl to a density of 1.550 g/cm³ and ethidium bromide to a concentration of 250 μ g/ml. (in a final volume of 2.5 ml.). Gradients were centrifuged for 24 h at 42,000 r.p.m., 20° C, in the SW 50 Spinco rotor. The position of supercoiled DNA molecules was checked against that of suitable markers (polyoma DNA, cellular nuclear DNA) running in parallel gradients. Graphs show ³H-thymidine incorporation into the mitochondrial DNA from infected (○) and uninfected (●) cells after CsCl-ethidium bromide gradient analysis. Peak I contains the supercoiled circles and peak II the relaxed circles and the linear molecules of mitochondrial DNA. The inset shows sucrose gradient analysis of cytoplasmic DNA from infected cells. The position of polyoma DNA was checked by parallel centrifugation of a mixture of labelled viral DNA and unlabelled cytoplasmic extract. Peak a indicates the position of the supercoiled circles of mitochondrial DNA (about 39S).

Table 1 Nuclear and Mitochondrial DNA Synthesis* in 2T3 Cells infected by Polyoma Virus

Experiment	State of the cells †	Radioactivity ‡ in nuclear DNA (%)		Radioactivity ‡ in mitochondrial DNA		
				Supercoiled (%)	Total	(%)
1	Confluent	5.35×10^5	(1.57)	524	1,194	(19)
	Growing	34×10^6	(100)	3,140	6,210	(100)
2	Confluent uninfected	3×10^5	(3.4)	360	622	(18.1)
	Confluent infected polyoma W.T.	8.6×10^6	(100)	2,835	3,425	(100)
3	Confluent uninfected	4.6×10^5	(3.9)	298	666	(16)
	Confluent infected polyoma ts 25	11.6×10^6	(100)	2,140	4,156	(100)
4	Confluent uninfected	5×10^5	(3.4)	598	1,127	(24.5)
	Confluent infected polyoma ts 25	14.7×10^6	(100)	2,292	4,581	(100)

* Determined from the incorporation of ^3H -thymidine.

† In experiment 1 cells were labelled for 3 h, in experiment 2 cells were labelled for 4 h, from 25 to 29 h after infection. In experiments 3 and 4 cells were labelled from 26 to 29 to 32 h after infection, respectively, at 38.5° .

‡ c.p.m./ 10^7 cells.

controlled level; only the block between the G_1 and the S phases in resting cells seems to be removed⁸. Several other physiological or artificial states, notably that resulting from differentiation in which cell DNA synthesis is suppressed, can be overcome by infection with such viruses^{8,9}. In any case the extent of stimulation seems to reach an absolute limit in the normal rate of cellular DNA replication during exponential growth.

The study of the effect of virus infection on extrachromosomal DNA synthesis bears some relevance to the understanding of both the regulation of cell DNA synthesis and the expression of viral functions. These experiments show that mitochondrial DNA synthesis is stimulated in contact-inhibited cultures of 3T3 mouse cells upon infection with polyoma virus.

Confluent cultures of 3T3 cells were infected with polyoma virus¹⁰ (multiplicity of infection, 100 p.f.u./cell), and incubated in conditioned medium¹¹ for the times desired. Mitochondrial DNA synthesis was measured by labelling the cells for 3–4 h with ^3H -thymidine, usually between 24 and 34 h after infection, when there was maximum stimulation of nuclear DNA synthesis^{1,10}. Mock-infected, identically treated cultures were always included in the experiments. In the conditions used, frequency of cells synthesizing DNA in the noninfected cultures never exceeded 1% and was generally of the order of 0.2%.

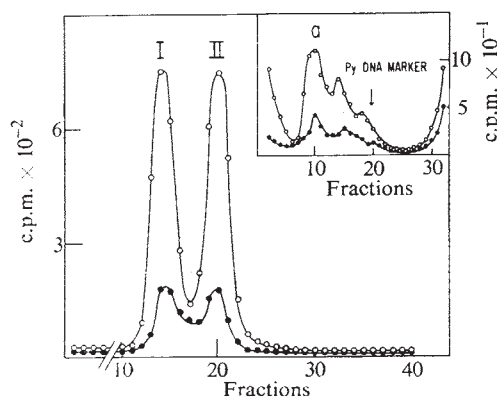


Fig. 2 Incorporation of ^3H -thymidine into the mitochondrial DNA of 3T3 cells infected with a ts-mutant of polyoma virus. 1.6×10^7 cells were infected with the ts 25 mutant of polyoma virus⁶ at a multiplicity of 100 p.f.u./cell, as described in Fig. 1, except that cells were kept at 38.5°C and exposed to ^3H -thymidine between the 29th and 32nd h after virus adsorption. Mitochondrial DNA was extracted and analysed as described in Fig. 1. Inset: Sedimentation in sucrose-SDS gradients of the DNA from the cytoplasmic extracts of infected and uninfected cells, labelled in the same conditions. The main graph shows CsCl-ethidium bromide gradient analysis of the DNA constrained in fractions 7–17 of the sucrose gradient shown in the inset. All other details are as in Fig. 1. ●, Mitochondrial DNA from infected cells; ○, mitochondrial DNA from control cells.

Fig. 1 illustrates the incorporation of ^3H -thymidine into the mitochondrial DNA of 3T3 cells labelled between 25 and 29 h after infection with wild type polyoma virus. Mitochondrial DNA was isolated from cytoplasmic extracts by zonal centrifugation in sucrose density gradients¹² (where any contaminating nuclear or viral DNA sediments faster or slower, respectively, than mitochondrial DNA) and then analysed in equilibrium CsCl-ethidium bromide gradients¹³.

The insert in Fig. 1 shows the radioactivity distribution obtained from the sucrose gradient centrifugation of the cytoplasmic extract of infected cells. Peak *a* has the sedimentation velocity of the intact supercoiled circles of mitochondrial DNA (about 39S, form I)¹⁴. The two smaller peaks to the right of *a* probably represent the other two forms of mitochondrial DNA, but the slowest one (about 20S) may represent the linear form of mitochondrial DNA or some viral DNA leaked out of the nuclei, or both. The fractions sedimenting faster than 21S were pooled and analysed by CsCl-ethidium bromide gradients (main graph in Fig. 1). Most of the radioactivity indeed seems to have been incorporated into twisted circular molecules of mitochondrial DNA. The same graph shows that the incorporation into a similarly treated sample from uninfected confluent cells is roughly six times lower.

In this experiment, the 20S peak of radioactivity was relatively small, so that its interference with an accurate estimation of labelled mitochondrial DNA could be considered negligible (the corresponding fractions were discarded). In other experiments with wild type virus, however, the leakage of supercoiled viral DNA from nuclei into the cytoplasmic extract was variable and generally larger. Thus, to prove unambiguously the specific induction of mitochondrial DNA synthesis, we carried out similar experiments with a conditional-lethal (ts) mutant of polyoma virus. Such a mutant, which grows at 31°C but cannot synthesize its DNA at 38.5°C , will still stimulate DNA synthesis in the host cells at that temperature⁶.

Fig. 2 shows the results of an experiment in which cells were infected with the ts-mutant (ts 25, supplied by Dr Di Mayorca⁶) at 38.5°C . The insert shows the radioactivity pattern obtained by centrifuging in sucrose gradients the cytoplasmic extracts from the infected and uninfected cultures. Peak *a* corresponds to about 39S; the radioactivity sedimenting faster than peak *a* is contaminating nuclear DNA¹² (discarded before the next step of the analysis). The rest of Fig. 2 shows the equilibrium-gradient analysis of the DNA precipitated from the central fractions of the sucrose gradients. The incorporation of radioactivity into mitochondrial DNA appears to be stimulated about four times by viral infection.

In this experiment the proportion of form I to the rest of mitochondrial DNA was smaller than in the previous experiment: this probably reflects a larger "nicking" occurred during the preparation of DNA.

Table 1 summarizes quantitatively the virus-induced effects on nuclear and mitochondrial DNA synthesis observed in

different experiments. The results indicate that the stimulation varies slightly from one experiment to another for both nuclei and mitochondria and that is smaller for mitochondrial than for nuclear DNA synthesis.

Although an intrinsically different sensitivity of the two synthetic systems to virus infection cannot be excluded, primary importance must be attributed, in interpreting these data, to the different levels of residual activity in the nuclei and mitochondria of resting cells. Table 1 shows the results of an experiment in which the DNA synthesis of confluent cultures was compared with that of growing cells. The nuclear activity seems to have been reduced by contact inhibition to less than 2% of that of multiplying cells, whereas the mitochondrial activity still proceeded at 20% the rate of exponentially growing cells. It is not possible at present to determine whether the 20% residual activity resulted from a portion of the cell population which escaped the population density block, or whether all cells synthesized mitochondrial DNA more slowly. The turnover of mitochondrial DNA apparently is higher in slow-growing than in fast-growing cells¹⁵. Moreover the cell population used in our experiments was quite homogeneous in all other respects, and even very prolonged incubation of the cells in state of contact-inhibition failed to reduce mitochondrial DNA synthesis beyond 15% of the rate of growing cells. These facts offer some support to the latter hypothesis. It is clear in any case that if the virus acts by triggering the mechanism responsible for the normal rate of DNA replication, the level of induction in the infected cells would be exactly the one we have found.

It seems therefore that polyoma virus can stimulate mitochondrial as well as nuclear DNA synthesis in cells in which DNA synthesis is repressed by contact inhibition. Furthermore, the experiments with the ts-mutant show that, as in the case of nuclear DNA synthesis, this effect does not require viral DNA replication, and must therefore be caused by a viral early function. Similar results have been obtained independently in another laboratory with SV40 infected cells¹⁶.

This work was carried out at New York University and was supported by grants from the American Cancer Society and the National Cancer Institute.

CESARE VESCO

Laboratory of Cell Biology of the CNR,
Rome

CLAUDIO BASILICO

Department of Pathology,
New York University School of Medicine,
New York,
New York 10016

Received January 4, 1971.

High Resolution Nuclear Magnetic Resonance Studies of Hydrogen Bonded Protons of tRNA in Water

SINCE the determination of their primary sequence the secondary and tertiary structures of tRNA molecules have been studied by various techniques (reviewed in ref. 1). In general, physical and chemical results, as well as the base homologies in different tRNA molecules, support Holley's "clover leaf" model². There is also evidence of tertiary structure, and different models have been suggested³. Because both secondary and tertiary structures depend on hydrogen bonding, it should be possible to determine molecular conformations in solution by studying the hydrogen bonds directly.

In previous high resolution proton nuclear magnetic resonance (NMR) studies of tRNA in D₂O, resonances of the non-exchangeable protons were measured and found to be rather poorly resolved⁴⁻⁶. NMR studies of complementary Watson-Crick pairs of nucleosides in non-aqueous polar solvents have shown that the exchangeable hydrogen bonded ring N-H protons of uridine and guanosine give sharper resonances at lower fields than the non-exchangeable protons^{7,8}. This suggested that it might be possible to observe and resolve the corresponding low field resonances from the relatively few hydrogen bonded protons of tRNA in aqueous solution.

In Fig. 1a and b the low field region of the 220 MHz NMR spectrum of unfractionated tRNA in H₂O is compared with that in D₂O. The peaks observed between -10 and -15 p.p.m. are more than twenty times weaker in the D₂O sample, indicating that they come from exchangeable protons. There is evidence of structure in Fig. 1a even though the sample was a mixture of many different tRNA molecules.

Fig. 2 illustrates the temperature dependence of the same spectral region for purified tRNA^{phe}_{yeast} in H₂O solution. In contrast to unfractionated tRNA at 24° C, the exchangeable proton spectrum of tRNA^{phe}_{yeast} is well resolved. In the narrowest resonance values of $\delta\nu_{1/2}$, the full line widths at half heights are ~50 Hz. The integrated intensity at 24° C of the peaks between -10 and -15 p.p.m. of this tRNA^{phe}_{yeast} sample was shown to correspond to 23 ± 3 exchangeable protons by an intensity comparison with the lowest field methyl resonance of cyanometmyoglobin⁹. When the temperature was increased, certain of these low field resonances were differentially broadened. For example, the -11 p.p.m. resonance broadened and disappeared just below 35° C whereas the -10.5 p.p.m. resonance did not begin to broaden until around 48° C, at which temperature a peak at -13.3 p.p.m. also broadened. The remaining resonances broadened between 59 and 61.5° C with the peak at -13.9 p.p.m. broadening last. At 61.5° C all

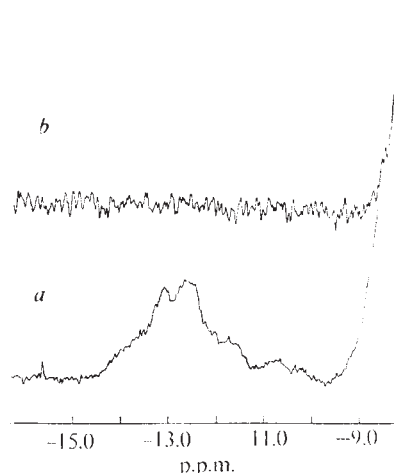


Fig. 1 The low field 220 MHz NMR spectra of unfractionated tRNA from 80 mg/ml. of yeast a, Sample in H₂O; b, sample dissolved in D₂O instead of H₂O.

- ¹ Dulbecco, R., Hartwell, L. H., and Vogt, M., *Proc. US Nat. Acad. Sci.*, **53**, 403 (1965).
- ² Weil, R., Michel, M. R., and Ruschmann, G. K., *Proc. US Nat. Acad. Sci.*, **53**, 1468 (1965).
- ³ Winocour, E., Kaye, A. M., and Stollar, V., *Virology*, **27**, 156 (1965).
- ⁴ Basilico, C., Marin, G., and Di Mayorca, G., *Proc. US Nat. Acad. Sci.*, **56**, 208 (1966).
- ⁵ Eckhart, W., *Virology*, **38**, 120 (1969).
- ⁶ Di Mayorca, G., Callender, J., and Giordano, R., *Virology*, **38**, 126 (1969).
- ⁷ Gershon, D., Hausen, P., Sachs, L., and Winocour, E., *Proc. US Nat. Acad. Sci.*, **54**, 1584 (1965).
- ⁸ Winocour, E., *Adv. Vir. Res.*, **14**, 153 (1969).
- ⁹ Yaffe, D., and Gershon, D., *Nature*, **215**, 421 (1967).
- ¹⁰ Basilico, C., Matsuya, Y., and Green, H., *J. Virol.*, **3**, 139 (1969).
- ¹¹ Todaro, G., Matsuya, Y., Bloom, S., Robbins, A., and Green, H., *Wistar Symp. Monogr.*, **7**, 87 (1967).
- ¹² Vesco, C., and Penman, S., *Biochem. Biophys. Res. Commun.*, **35**, 249 (1969).
- ¹³ Radloff, R., Bauer, W., and Vinograd, J., *Proc. US Nat. Acad. Sci.*, **57**, 1514 (1967).
- ¹⁴ Borst, P., Van Bruggen, E. F. J., Ruttenberg, G. J., and Kroon, A. M., *Biochim. Biophys. Acta*, **149**, 156 (1967).
- ¹⁵ Nass, M. M. K., *Science*, **165**, 25 (1969).
- ¹⁶ Levine, A., *Proc. US Nat. Acad. Sci.* (in the press).

peaks between -10 and -15 p.p.m. disappeared in accordance with the melting curve of tRNA^{phe}_{yeast} (ref. 10). When the temperature was lowered the original spectra in this region were recovered. No detectable changes in this region were observed with the addition of an excess of (Up)₅U, which contains the codon triplet, probably because the sticking time of this codon is not long enough to give narrow resonances.

Both the unfractionated tRNA and the tRNA^{phe}_{yeast} were purchased from Boehringer-Mannheim and dissolved in distilled water without any purification. The salt concentrations in the NMR samples, extrapolated from conductivity measurements made on dilute solutions, were about 0.4 M equivalents of NaCl. We are studying the effects of divalent metal ions on the state of tRNA at these high concentrations, for they are known to affect the properties of tRNA when applied in lower concentration, presumably by causing changes in conformation¹⁰⁻¹⁵.

When the tRNA^{phe}_{yeast} samples were diluted to 30 mg/ml. the only change in the spectrum was a decrease in the signal to noise ratio. With the dilute sample it was necessary to accumulate spectral data for 12 h, whereas 4 h accumulation was the average for the spectra shown here. Broad lines were observed when we used concentrations greater than 100 mg/ml., probably because of the obviously high viscosity. As in other large molecules, the line widths at 80 mg/ml. seem to be determined by incomplete averaging of the nuclear dipolar interaction by the molecular rotation. The absolute values of the line widths and their constancy when tRNA was diluted and after melting suggest that the tRNA^{phe}_{yeast} molecules are not aggregated.

As the temperature increases, uncertainty broadening dominates the line widths so that $\tau_s = (\pi\delta\nu_{1/2})^{-1}$ where τ_s is the sticking time of the hydrogen bond. Thus for the observed values of $\delta\nu_{1/2} \approx 50$ Hz the uncertainty broadening became comparable with the dipolar broadening when $\tau_s \approx 6$ ms. In the tRNA^{phe}_{yeast} spectrum this means that τ_s of one proton (near -11 p.p.m.) is about 2 ms at 24°C and is considerably shorter at 35°C. Between 35 and 48°C, τ_s becomes shorter than 6 ms for the resonances at -10.5 and -13.3 p.p.m.

The N₃ proton of uridine gives a peak at -7.9 p.p.m. in DMSO which is shifted to about -11.0 p.p.m. when hydrogen is bonded with adenosine⁷. Similarly, the N₁ proton of guanosine shifts from -10.5 p.p.m. in DMSO to about

-12.5 p.p.m. when hydrogen is bonded with cytosine⁷. Since hydrogen bonding does not shift amino protons nearly as far down field as the N-H ring protons, we assume that in tRNA only N-H ring protons will be observed in the -12 to -15 p.p.m. region. On this basis, each Watson-Crick base pair should contribute only one proton to resonances below -12 p.p.m., and so the 21 ± 3 protons observed in this region in tRNA^{phe}_{yeast} agree well with the clover leaf model which has twenty-one base pairs if one G-U pair is included. The two additional protons contributing to the peaks between -10 and -12 p.p.m. are neglected in this assignment because they may be amino protons. If they are ring protons then the spectra indicate the existence of 23 ± 3 base pairs. Englander and Englander¹⁶ found an approximately equivalent number of slowly exchanging protons in tritium exchange measurements on unfractionated tRNA. NMR studies of model systems have shown that there is a linear relation between the enthalpy of the hydrogen bond and the resonance shift to lower fields¹⁷. When the individual resonances of tRNA are assigned it should be possible to determine the strengths and sticking times of individual hydrogen bonds.

D. R. K. is a John Simon Guggenheim Fellow.

DAVID R. KEARNS*
DINSHAW J. PATEL
R. G. SHULMAN

Bell Telephone Laboratories Inc.,
Murray Hill,
New Jersey 07974

Received July 9; revised August 3, 1970.

* Present address: Department of Chemistry, University of California, Riverside, California.

- ¹ Zachau, H. G., *Angew. Chem. Intern.*, ed., **8**, 711 (1969).
- ² Holley, R. W., Apgar, J., Everett, G. A., Madison, J. T., Marquisee, M., Merrill, S. H., Penswick, J. R., and Zamir, A., *Science*, **147**, 1462 (1965).
- ³ Levitt, M., *Nature*, **224**, 759 (1969).
- ⁴ McTague, J. P., Ross, V., and Gibbs, J. H., *Biopolymers*, **2**, 163 (1964).
- ⁵ McDonald, C. C., Phillips, W. D., and Penswick, J. R., *Biopolymers*, **3**, 609 (1965).
- ⁶ Smith, I. C. P., Yamane, T., and Shulman, R. G., *Canad. J. Biochem.*, **47**, 480 (1969).
- ⁷ Katz, L., and Penman, S., *J. Mol. Biol.*, **15**, 220 (1966).
- ⁸ Shoup, R. R., Miles, H. T., and Becker, E. D., *Biochem. Biophys. Res. Commun.*, **23**, 194 (1966).
- ⁹ Wüthrich, K., Shulman, R. G., and Peisach, J., *Proc. US Nat. Acad. Sci.*, **60**, 373 (1968).
- ¹⁰ Cramer, F., Doepner, H., Haar, F. v. d., Schlimme, E., and Seidel, H., *Proc. US Nat. Acad. Sci.*, **61**, 1384 (1968).
- ¹¹ Fresco, J. R., Adams, A., Ascione, R., Henley, D., and Lindahl, T., *Cold Spring Harbor Symp. Quant. Biol.*, **31**, 527 (1966).
- ¹² Vournakis, J. N., and Scheraga, H. A., *Biochemistry*, **5**, 2997 (1966).
- ¹³ Eisinger, J., Feuer, B., and Yamane, T., *Proc. US Nat. Acad. Sci.*, **65**, 638 (1970).
- ¹⁴ Zimmerman, T. P., Robison, B., and Gibbs, J. H., *Biochim. Biophys. Acta*, **209**, 151 (1970).
- ¹⁵ Schulman, L. D., and Chambers, R. W., *Proc. US Nat. Acad. Sci.*, **61**, 308 (1968).
- ¹⁶ Englander, S. W., and Englander, J. J., *Proc. US Nat. Acad. Sci.*, **53**, 370 (1965).
- ¹⁷ Eymann, D. P., and Drago, R. S., *J. Amer. Chem. Soc.*, **88**, 1617 (1966).

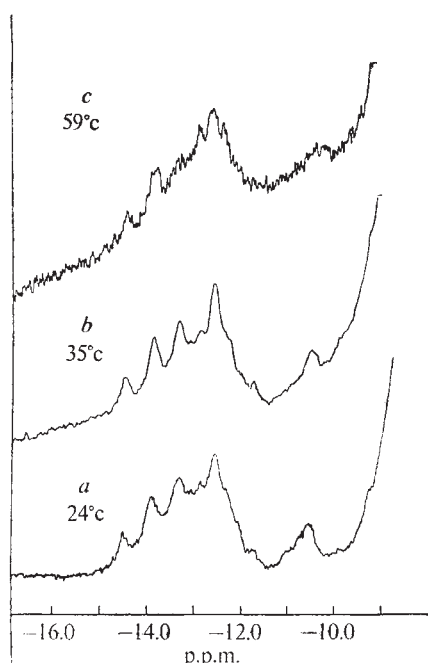


Fig. 2 The low field 220 MHz NMR spectra of 80 mg/ml. of tRNA^{phe}_{yeast}. Temperatures at which each spectrum were recorded are indicated.

Early DNA Replication Patterns of the Normal Sex Chromosomes and a Presumptive X-autosome Translocation in Cattle (*Bos taurus* L.)

THE late DNA replication pattern of one sex chromosome in mammals is well known from studies of various species, including cattle¹⁻³. The replication pattern of structurally

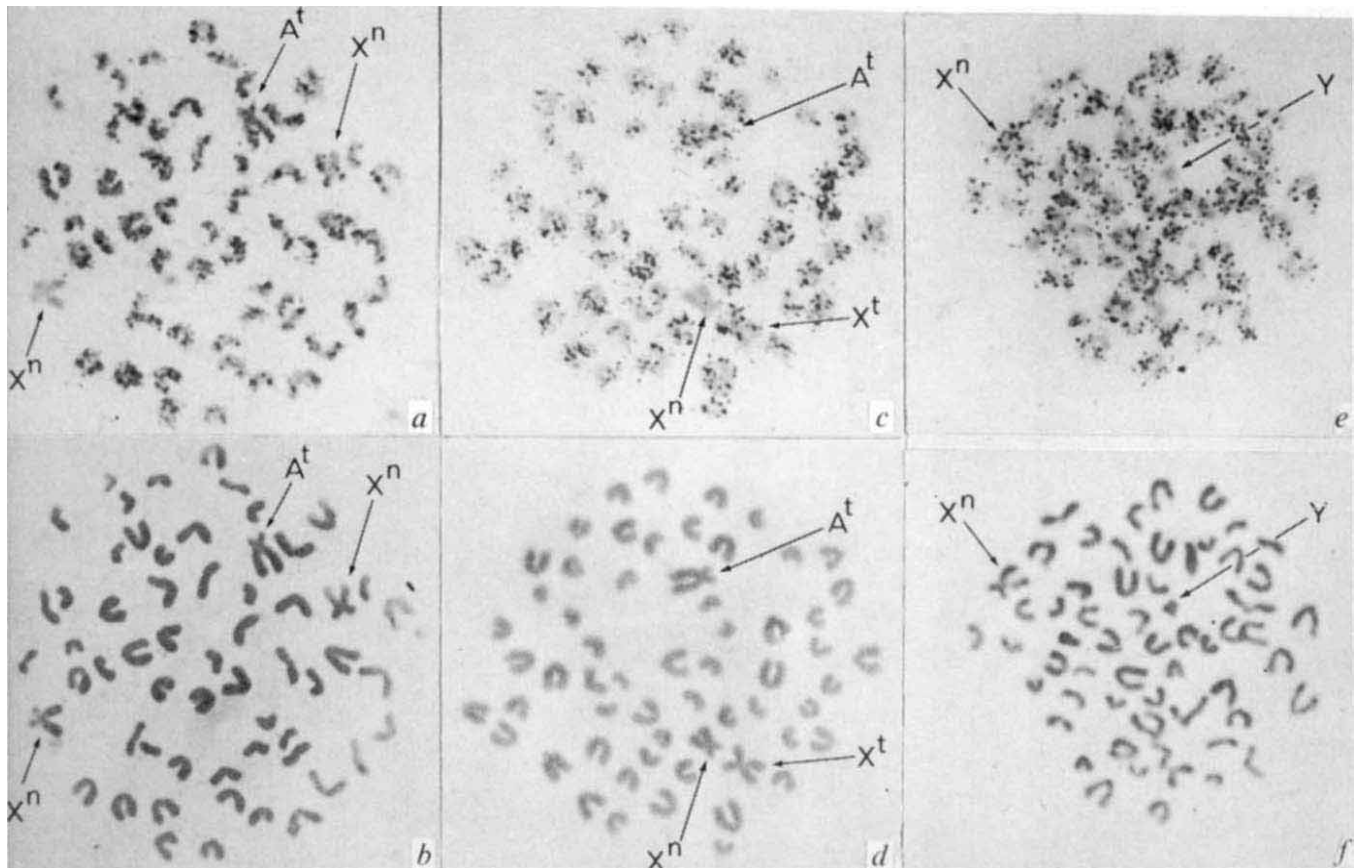


Fig. 1 *a*, Metaphase of the female heterozygous for the autosomal translocation ($X^n/X^t, A^t/-$). All chromosomes except one X are heavily labelled (pulse-labelling according to Hsu and Lockhart¹¹). The X s and A^t are indicated. *b*, The same metaphase as *a* after removal of the autoradiographic grains. *c*, Metaphase of the female heterozygous for the autosomal and the presumptive X -autosome translocation ($X^n/X^t, A^t/-$). All chromosomes except X^n are heavily labelled (labelling according to Mukherjee *et al.*¹²). The X^t and A^t chromosomes are also indicated. *d*, The same metaphase as *c* after removal of the autoradiographic grains. *e*, Metaphase of the normal male. All chromosomes except Y are labelled (pulse-labelling according to Hsu and Lockhart¹¹). *f*, The same metaphase as *e* after removal of the autoradiographic grains.

rearranged sex chromosomes has also been described for several species. In most cases the postulated random inactivation of the X in the single female seems to be disturbed. This is the case with several X chromosome rearrangements in man⁴, Searle's translocation in the mouse⁵ and a presumptive X -autosome translocation in cattle³. I have investigated the early DNA replication pattern of the normal sex chromosomes in cattle and the presumptive X -autosome translocation.

My subjects were two females and one male. The two females had a diploid chromosome number of 59; the reduction from the normal 60 was the result of a translocation of centric fusion type^{6,7}. One of the females had a normal sex chromosome set (X^n/X^n), the other was heterozygous for a presumptive X -autosome translocation (X^n/X^t). The male had a diploid number of 60 with normal sex chromosomes.

Blood was cultured by the methods of Moorhead *et al.*⁸ and Arakaki and Sparkes⁹. Tritiated thymidine (specific activity 5.0 and 7.2 Ci/mmol) was added to a final concentration of 1 μ Ci/ml. Preparations were made by the air-drying technique¹⁰ and Kodak 'AR 10' stripping film was applied to each slide. After exposure for about 11 days the slides with the film were developed, stained in Giemsa and mounted in 'Euparal'. Suitable metaphase figures were analysed and photographed. Then coverslips were removed, the stripping film was hydrolysed and the preparations were mounted. The metaphase figures were rephotographed and compared with photographs of the labelled metaphase figures.

Two methods were used for the study of DNA synthesis. According to the method of Hsu and Lockhart¹¹, cells were pulse-labelled for 20 min, approximately 9 h before collection. After treatment with the isotope cells were washed twice in tissue

culture medium containing a high concentration of unlabelled thymidine. 'Colcemid' (Ciba) was added approximately 2 h before cells were collected. According to the method of Mukherjee *et al.*¹² tritiated thymidine was added to cultures 0–16 h after incubation. Cells were washed in tissue culture medium 52 h–68 h after incubation and colchicine was added 1 h after washing. After 70–75 h of incubation cells were collected.

By these methods^{11,12} approximately 400 and 200 cells, respectively, were analysed from each animal. Percentages of metaphases labelled, metaphases with only one chromosome unlabelled and metaphases totally labelled are given in Table 1.

Labelled metaphases with one "cold" chromosome were never covered by less than 300 grains. The "cold" chromosome was nearly always the normal X , both in the female with normal X chromosomes ($X^n/X^n, A^t/-$) and in the female heterozygous for the presumptive X -autosome translocation ($X^n/X^t, A^t/-$) (Fig. 1 *a, b, c*, and *d*). Only in 1% of the pooled material was the "cold" chromosome(s) a single or a very few small autosome(s).

From heavily labelled cells it could be seen that the short arm was the last part of the late X to initiate replication. The same pattern was seen in the A^t ; the synthesis of the short arm always initiated later than that of the long arm. The presumptive X -autosome translocation (X^t) was consequently "hot" in all cells analysed in the heterozygous female ($X^n/X^t, A^t/-$).

In cells with more than one unlabelled chromosome, the number of grains was less than 300. These figures are not included in Table 1.

The Y chromosome had a replication pattern similar to the normal X , that is it was "cold" during the early stage of the S phase (Fig. 1 *e* and *f*).

Table 1 Labelling of Metaphase Figures

Animals	% metaphases labelled	Labelling methods				
		Hsu and Lockhart ¹¹ % labelled metaphases with one chromosome unlabelled	% metaphases with all chromosomes labelled	% metaphases labelled	Mukherjee <i>et al.</i> ¹² % labelled metaphases with one chromosome unlabelled	% metaphases with all chromosomes labelled
$X^n/X^n, A^1/-$	98.07	62.90	31.98	85.09	28.24	56.09
$X^n/X^1, A^1/-$	94.50	53.35	21.55	94.09	18.86	73.52
X^n/Y	98.07	56.02	31.73	91.37	10.44	77.94

The high frequency of female cells which incorporated no tritium into one X chromosome although otherwise incorporation was strong, suggests that there is an asynchronous replication pattern of the X chromosome at the beginning of DNA synthesis. This agrees well with results from studies of cattle² and other species such as man¹³, but deviates from those of Mukherjee *et al.*¹² with cattle, although both the pulse-labelling technique of Hsu and Lockhart¹¹ and the method elaborated by Mukherjee *et al.*¹² were used. Differences in results when the two methods are used may arise because cultured leucocytes sometimes divide twice or three times before they are collected¹³. This, however, cannot explain the results obtained from cattle by Mukherjee *et al.*¹². They found that at least twelve autosomes remain unlabelled when both X chromosomes have already started replication. They also suggested that the two X chromosomes start replication within a very short time, but after a short time synthesis stops in one of the X chromosomes, followed by a burst in DNA synthesis during the last part of the S phase.

My results clearly indicate that one of the X chromosomes in female cattle starts to replicate later than the other chromosomes of the complement; similarly the Y chromosome is the last chromosome to initiate replication in the normal male.

This work was supported by the Swedish Agricultural Research Council and the Swedish Natural Research Council.

INGEMAR GUSTAVSSON

Department of Animal Genetics,
Nutrition and Hygiene,
Royal Veterinary College,
Stockholm

Received October 16, 1969; revised September 25, 1970.

¹ Mukherjee, B. B., and Sinha, A. K., *Canad. J. Genet. Cytol.*, **5**, 490 (1963).

² Gartler, S. M., and Burt, B., *Cytogenetics*, **3**, 135 (1964).

³ Gustavsson, I., Fraccaro, M., Tiepolo, L., and Lindsten, J., *Nature*, **218**, 183 (1968).

⁴ Fraccaro, M., and Lindsten, J., in *Cytogenetics of Cells in Culture* (edit. by Harris, R. J. C.) (Academic Press, New York, 1964).

⁵ Ohno, S., and Lyon, M. F., *Chromosoma*, **16**, 90 (1964).

⁶ Gustavsson, I., *Nature*, **211**, 865 (1966).

⁷ Gustavsson, I., *Hereditas*, **63**, 68 (1969).

⁸ Moorhead, P. S., Nowell, P. C., Mellman, W. J., Battips, D. M., and Hungerford, D. A., *Exp. Cell Res.*, **20**, 613 (1960).

⁹ Arakaki, D. T., and Sparkes, R. S., *Cytogenetics*, **2**, 57 (1963).

¹⁰ Rothfels, K. H., and Siminovich, L., *Stain Tech.*, **33**, 73 (1957).

¹¹ Hsu, T. C., and Lockhart, L. H., *Hereditas*, **52**, 320 (1964).

¹² Mukherjee, B. B., Sinha, A. K., Mann, K. E., Ghosal, S. K., and Wright, W. C., *Nature*, **214**, 710 (1967).

¹³ Takagi, N., and Sandberg, A. A., *Cytogenetics*, **7**, 135 (1968).

occurs. Although these events immediately precede the initiation of differentiation, an interrelationship between proliferation and differentiation has not been demonstrated. Because of the stimulation, the chick embryo epidermis at days 11–14 is five-fold more active mitotically than the terminal embryonic or post-embryonic chick epidermis¹. The same stimulus or stimuli may also be related to the induction of DNA polymerase found during days 10–13 (ref. 2), an event which precedes the increase in DNA synthesis during this period. This increase was verified³ by *in vitro* experiments in which 2-¹⁴C-thymidine was incorporated into the DNA of cultured chick embryo skin. Both the epidermis and dermis of the day 14 embryonic skin show similar stimulation of DNA synthesis compared with synthesis in the day 19 embryonic skin. The study of DNA synthesis in the chick embryo skin is therefore of considerable interest because it encompasses both the stimulatory and inhibitory stages of synthesis. We here report the variation of DNA synthesis in the chick embryonic skin as a function of age (embryonic) as a way of clarifying these events before further investigation of the natural stimulants and inhibitors of DNA synthesis and their influences on the epidermal cell cycle.

Skin was obtained from the shank of white leghorn chick embryos, age 12 to 21 days. The large toe was measured and the embryo skin used experimentally only if its measurements were within the prescribed limits⁴. The skin was cultured as described previously³ with some modification as described below. The 1 ml. of culture medium per incubation contained 0.6 μ Ci of 2-¹⁴C-thymidine (specific activity 53 mCi/mmol; New England Nuclear Corporation).

After addition of the skin and medium to the dishes, the culture dishes were placed in an airtight 'Lucite' box (designed and fabricated by the NIH instrument shop), aerated for about 3 min with a gas mixture of 95% air–5% CO₂, sealed, and incubated at 37° C for the 4 h. The incubations were terminated by immersing the tissue in 0.5 ml. of 10% trichloroacetic acid (TCA) at 4° C.

DNA was isolated by a modification of the method of Schmidt and Thannhauser⁶, and of the 1.2 ml. obtained after hot TCA (90° C 5%) extraction, aliquots of 0.35 ml. were assayed in duplicate by the diphenylamine reaction of Burton⁷ and radioactivity was measured in duplicate by adding 0.1 ml. aliquots to a toluene–cellosolve scintillation fluid (PPO–POPOP) and counting in a Packard 'Tri-Carb' liquid scintillation spectrometer, model 3375. Specific activity was calculated as total c.p.m. of the isolated DNA per absorbance unit. The data presented are the averages of triplicate experiments.

The rate of 2-¹⁴C-thymidine incorporation into skin DNA of ages 12–21 days varied as shown in Fig. 1. The peak specific activity at the thirteenth day is about 15-fold the minimal incorporation found at the end of pre-natal life (day 21). The decline in specific activity is almost linear between days 14 and 18.

In adult epidermis it has been suggested that the initiation of the cell cycle is related to the process of desquamation. This thesis is based on the observations that removal of the topmost stratum corneum layers results in the basal cells responding with an increased mitotic rate^{12–14}.

Variation of DNA Synthesis with Age in Chick Embryo Skin

THE embryonic epidermis maintains a two or three cell layer population of undifferentiated cells for several days before about the eleventh day when a sudden burst of proliferation

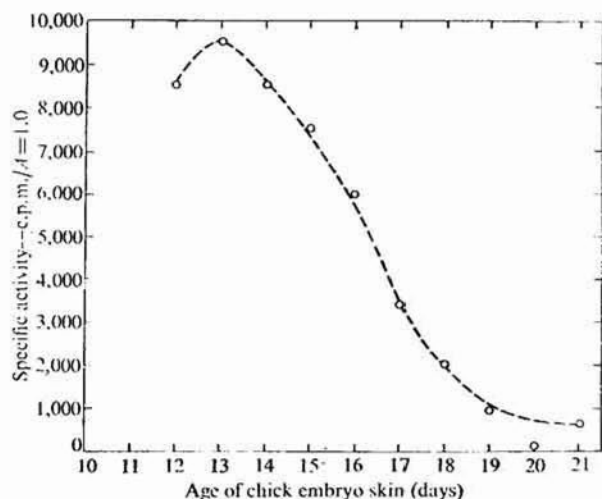


Fig. 1 Variation of $2\text{-}^{14}\text{C}$ -thymidine incorporation into chick embryonic skin DNA with skin embryonic age.

Because the first cycle of keratinization is complete at about the eighteenth day⁹⁻¹¹ with the appearance of stratum corneum, simultaneous with the shedding of the periderm layer, this mechanism seems unlikely to account for the stimulation of DNA synthesis activity at days 12-14. The stimulation occurs before both the formation of the stratum corneum and the beginning of differentiation in the lower layers of the epidermis.

Although the stimulation of DNA synthesis seems important to the formation of a multicell layered epidermis, there is no immediate explanation why peak DNA synthesis during days 12-14 is not sustained. One possible explanation for the termination of peak synthesis is that an epidermal inhibitor, the chalone substance of Bullough and co-workers^{15,16}, although inactive during the earlier embryonic days when the burst of DNA synthesis occurs, is either activated or synthesized in the final days of embryonic life.

Although the epidermal chalone does not inhibit DNA synthesis in incubations of 1-3 h¹⁷, an inhibition was found 9-12 h after addition of the chalone extract¹⁸. This suggests, therefore, that the action of the chalone substance occurs at other than the S_1 period of the cell cycle.

Another possibility is that a macromolecule similar to the epidermal growth factor (EGF)¹⁹ is responsible for the beginning of keratinization at day 13. How and if the EGF influences the burst of DNA synthesis at this point is unclear, for no accumulation of DNA results when EGF is added to cultured chick embryo epidermis²⁰. The action of EGF was found to increase amino-acid incorporation by increased binding of messenger RNA to polysomal RNA^{21,22}.

SIMON ROTHBERG*
THOMAS M. EKEL*

Dermatology Branch,
National Cancer Institute,
National Institutes of Health,
Bethesda,
Maryland 20014

Received May 22; revised August 18, 1970.

* Present address Division of Dermatology, Medical College of Virginia—the Health Sciences Division of Virginia Commonwealth University, Richmond, Virginia 23219.

- ¹ Rothberg, S., and Ekel, T., *Nature*, **216**, 1352 (1967).
- ² Kischer, C. W., and Furlong, B., *Proc. Soc. Exp. Biol.*, **124**, 1188 (1967).
- ³ Kierney, C. E., and Rothberg, S., *J. Invest. Dermatol.*, **53**, 351 (1969).
- ⁴ Hamburger, V., and Hamilton, H., *J. Morphol.*, **88**, 49 (1951).
- ⁵ Rothberg, S., *J. Invest. Dermatol.*, **49**, 35 (1967).

- ⁶ Munro, H. N., and Fleck, A., *Meth. Biochem. Analysis*, **14** (edit. by Glick, D.) (Wiley, New York, 1966).
- ⁷ Burton, K., *Biochem. J.*, **62**, 315 (1956).
- ⁸ Fitton Jackson, S., and Fell, H. B., *Develop. Biol.*, **7**, 394 (1963).
- ⁹ Wessells, N. K., *Develop. Biol.*, **3**, 355 (1961).
- ¹⁰ Wessells, N. K., *New Engl. J. Med.*, **277**, 21 (1967).
- ¹¹ Parakaal, P. F., and Matoltsy, A. G., *J. Ultrastruct. Res.*, **23**, 403 (1968).
- ¹² Pincus, H., *J. Invest. Dermatol.*, **19**, 431 (1952).
- ¹³ Brophy, D., and Lobitz, jun., W. C., *J. Invest. Dermatol.*, **32**, 495 (1959).
- ¹⁴ Christophers, E., and Braun-Falco, O., *Arch. Klin. Exp. Dermatol.*, **231**, 85 (1967).
- ¹⁵ Bullough, W. S., and Lawrence, E. B., *Exp. Cell Res.*, **33**, 176 (1964).
- ¹⁶ Bullough, W. S., and Lawrence, E. B., *Symp. Zoological Soc. London*, No. 12 (edit. by Ebling, F.) (Academic Press, London, 1964).
- ¹⁷ Baden, H. P., and Sviokla, S., *Exp. Cell Res.*, **50**, 644 (1968).
- ¹⁸ Hennings, H., Elgjo, K., and Iversen, O. H., *Virchows Arch.*, **4**, 45 (1969).
- ¹⁹ Cohen, S., *Develop. Biol.*, **3**, 394 (1965).
- ²⁰ Hooper, J. K., and Cohen, S., *Biochim. Biophys. Acta*, **138**, 347 (1967).
- ²¹ Hooper, J. K., and Cohen, S., *Biochim. Biophys. Acta*, **138**, 357 (1967).
- ²² Cohen, S., and Stastny, M., *Biochim. Biophys. Acta*, **166**, 427 (1968).

Strains of Bovine Enterovirus sharing Antigen with Polio Virus-2

CATTLE are known to carry a substance(s) in their sera which specifically neutralizes various strains of polio virus¹. It has been thought that the production of this neutralizing substance might be due to infection of the cattle with some other virus sharing a common antigen with the polio virus. No such agent, however, has so far been discovered.

Eleven strains of bovine enterovirus (strains No. 145, 172, 185, 208, 213, 221, 333, 334, 335, 337 and 342) were isolated from the stools of calves using primary culture from rhesus monkey kidney cell (N. N., S. B., and L. N. M., unpublished). Of the eleven strains isolated strains 208 and 213 were of special interest and are the subject of this report. The two strains were resistant to ether, chloroform and deoxycholate, stable at pH 3.0 and heat stable in the presence of magnesium chloride. They measured 30-31 nm and were not inhibited in the presence of 10^{-5} mol/ml. of 5-iodo-2'-deoxyuridine. They had a cytopathic effect (CPE) of the polio virus type on primary culture of rhesus monkey, guinea-pig, rabbit and buffalo-calf kidney cell. A similar CPE was also seen on mouse and chick embryo cell cultures. Further, strains 208 and 213 produced a CPE on the HEP-2 cell line. Neither was pathogenic to infant and adult mice, guinea-pigs or rabbits, but they were fatal to developing chicken embryo when inoculated by the allantoic route.

Strain Nos. 208 and 213 were antigenically identical. They were not neutralized by the bovine enterovirus antisera of Laplace³ groups 1 and 2, Burki⁴ 51/60, 100/60, 256/60 and 328/60. Antisera against polio virus-1, 3 echovirus 1, 2, 3, 4, 5, 6, 7, 11, 12, 13, 15, 18, 19, 21, Coxsackie virus B-1, 2, 4, 5 and 6 did not neutralize the two strains. 100 TCID₅₀ of the two strains were, however, neutralized by 20 neutralizing units of polio virus-2 antiserum. Twenty neutralizing units of antisera against strains 208 and 213 raised in fowls neutralized 100 TCID₅₀ of polio virus-2. Twenty neutralizing units of antisera raised against strain Nos. 208 and 213 neutralized 100 TCID₅₀ of strain Nos. 146, 172, 185, 221, 333, 334, 335, 337 and 342.

Sharing of antigen(s) between bovine enterovirus strains BEV-1 and BEV-180 and infectious bovine rhinotracheitis (IBR) virus has been reported⁵ but this is the first time that a common antigen(s) between human and bovine enterovirus has been reported. It is possible that the strains described

and other similar ones might be responsible for the presence of "antibodies" against human enteroviruses in bovine sera.

N. NATH
S. BALAYA
L. N. MOHAPATRA

Department of Microbiology,
All India Institute of Medical Sciences,
New Delhi-16

Received May 19, 1970.

¹ Hammon, W. McD., Mack, W. N., and Reeves, W. C., *J. Immunol.*, **57**, 285 (1947).

² Bartell, P., and Klein, M., *Proc. Soc. Exp. Biol. Med.*, **90**, 597 (1955).

³ Laplace, M., Portolani, A. M., and Lamieri, C., *Arch. Ges. Virusforsch.*, **17**, 98 (1965).

⁴ Burki, F., *Zbl. Vet. Med.*, **9**, 999 (1962).

⁵ Moll, T., and Davis, A. D., *Amer. J. Vet. Res.*, **20**, 27 (1959).

Human Blastocyst grown *in vitro* in Ovulation Cervical Mucus

HUMAN spermatozoa invariably live longer in ovulation cervical mucus than in their own seminal fluid. This can be observed in slide cover glass or capillary tube preparations. At ovulation the cervical mucus is most abundant, possesses the lowest viscosity or *spinnbarkeit*, is most translucent, contains the highest water concentration and fewest cells, is most alkaline, permits maximum spermatozoan penetration, contains the maximum of glycogen, maltose, mannose, fructose, fucose, hexosamine, glutamic acid, taurine, methionine, lysine, aspartic acid, glycine, alanine, valine, serine, arginine, cholesterol, lipid, phosphorus, and sodium chloride. It possesses thromboplastic activity and is bacteriostatic. Blood group substances corresponding to the blood group of the individual occur in the cervical secretion in high titre if the person is a secretor¹.

An ovum was aspirated from its follicle in the follicular fluid by means of a sterile 5 ml. syringe and an 18 gauge needle passed through the ovarian tissue 2 mm from the edge of the follicle, then into it posteriorly to prevent leakage. This is the method used for obtaining follicular oocytes and ova for previous studies on *in vitro* fertilization and cleavage²⁻⁸. The ovum was taken from a 34 yr old patient undergoing laparotomy for fibromyomata uteri, on the fourteenth day of a regular 28 day menstrual cycle. It was kept in the follicular fluid at body temperature.

After the abdomen was closed, the patient was placed in the modified lithotomy position, the portio of the cervix exposed and cleansed with a cotton swab. With a sterile 5 ml. syringe and a bevelled 16 gauge needle 1.2 ml. of the watery, clear cervical mucus was aspirated from the mid-cervical canal, after which it was expressed into a sterile Petri dish. The ovum in its follicular fluid was then expressed into the cervical mucus and identified under the dissecting microscope. It was mature in that the first polar body could be made out clearly through the sufficiently translucent corona cells. A ring of 'Vaseline' was placed around the preparation to prevent it from spreading. A drop of semen from the husband with normal spermatozoan count and morphology was added to the preparation, and finally very small pieces of the tubal fimbriae. The Petri dish was covered, placed in a moist chamber in the presence of 20% oxygen, and kept at body temperature. The primary objective was to simulate the natural environment as much as possible.

After 5 days of incubation the ovum was in the blastocyst stage. The criteria and those used previously concerning fertilization were the same as those cited by Edwards *et al.*⁹. The blastocyst was then transferred by means of a capillary pipette filled with physiological saline onto a glass slide,

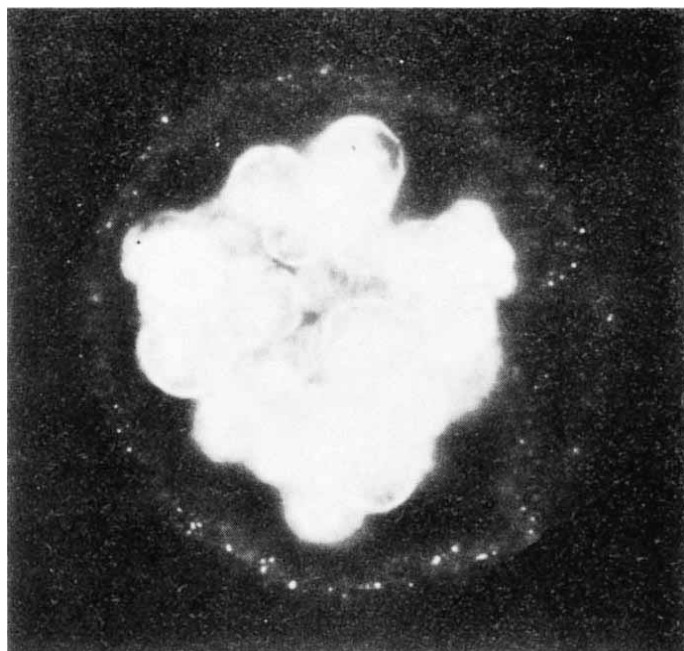


Fig. 1 Human blastocyst grown in ovulation phase cervical mucus 5 days after fertilization. (Phase contrast, $\times 240$.)

covered with a cover glass supported and sealed with a 'Vaseline' ring. It was photographed in phase contrast (Fig. 1).

The grossly normal blastocyst of approximately 100 cells, shown in optical section, was not transferred *in utero* in that the patient was only 5 days post-multiple myomectomies. Otherwise, there was no discernible contraindication for a successful transfer *in vitro* and continued development. This is scheduled for patients with ligated or excised fallopian tubes who may want a child, with the ova obtained by culdoscopy or laparoscopy.

LANDRUM B. SHETTLES

Department of Obstetrics and Gynecology,
College of Physicians and Surgeons of Columbia University,
New York

Received November 13, 1970.

¹ Shettles, L. B., *J. Reprod. Med.*, **3**, 43 (1969).

² Shettles, L. B., *Amer. J. Obstet. Gynec.*, **66**, 235 (1953).

³ Shettles, L. B., *Trans. NY Acad. Sci.*, **17**, 99 (1955).

⁴ Shettles, L. B., *Amer. J. Obstet. Gynec.*, **76**, 398 (1958).

⁵ Shettles, L. B., *Ovum Humanum* (Urban and Schwarzenberg, Munich, 1960).

⁶ Shettles, L. B., *Obstet. Gynec.*, **20**, 750 (1962).

⁷ Shettles, L. B., *Bull. Sloane Hospital for Women*, **10**, 246 (1964).

⁸ Shettles, L. B., in *Scientific Foundations of Obstetrics and Gynecology* (edit. by Philipp, E. E., Barnes, J., and Newton, M.) (Heinemann, London, 1970).

⁹ Edwards, R. G., Steptoe, P. C., and Purdy, J. M., *Nature*, **227**, 1307 (1970).

Capacitation of Hamster Spermatozoa by β -Glucuronidase

CAPACITATION, or the ability for immediate penetration of the ovum, occurs when epididymal sperm of the golden hamster (*Mesocricetus auratus*) are incubated in the presence of follicular fluid¹⁻³. Yanagimachi has reported that sperm motility is maintained by a dialysate of detoxified bovine follicular fluid, but capacitation of the sperm does not occur unless a water-soluble non-dialysable fraction is also provided⁴. The chemical nature of these factors has not yet been determined. Because ovarian follicles, particularly those in atresia, are known to

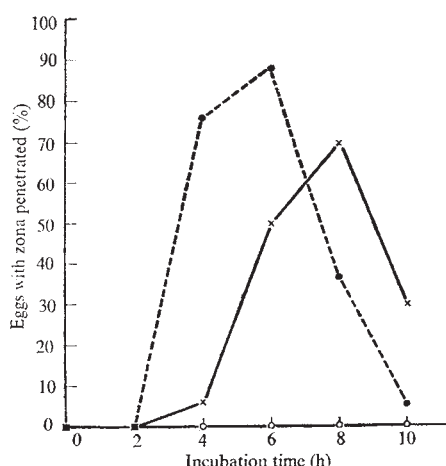


Fig. 1 Capacitation of golden hamster sperm by β -glucuronidase (2 Fishman units/ml.) ($\times$ — $\times$) and oviduct contents (17 h after HCG) ($\bullet$ — $\bullet$). Points on abscissa show the failure of medium 199 M alone to induce capacitation.

contain lysosomal enzymes⁵, we investigated the effect of a lysosomal preparation from beef liver on hamster epididymal sperm. Finding a striking stimulation of motility and capacitation of the sperm, we went on to test the lysosomal enzyme, β -glucuronidase, which is widely distributed in mammalian tissue including cells of the ovarian follicle⁶. We found that this enzyme duplicated the effect of the lysosomal preparation, as we shall now describe.

Hamster epididymal sperm were collected in medium 199 M as reported previously⁷. Drops (20 μ l.) of a sperm suspension (10^7 motile sperm/ml.) were added under mineral oil to equal volumes of 199 M, containing either the contents of an oviduct 17 h after administration of human chorionadotrophin (HCG) or β -glucuronidase (20 μ g or 2 Fishman units/ml. beef liver preparation from Nutritional Biochemical Corp.). Previous studies had shown that this concentration of the enzyme was optimal for capacitation. At various intervals eggs introduced with the oviduct contents were removed with a micropipette and twenty cumulus-free eggs were added to each drop. Cumulus was removed with hyaluronidase (450 USP units/ml. of phosphate buffered saline containing 1% polyvinylpyrrolidone). After incubation for another 90 min, eggs were transferred to a slide, compressed slightly under a 'Vaseline'-edged cover glass and examined under a phase contrast microscope for sperm penetration of the zona pellucida.

We reported earlier that incubation in medium alone caused fertilization of 2% of the ova added to the sperm suspension³. Numerous other experiments have now shown that capacitation in 199 M alone is erratic and results in the penetration of 0 to 5% of the eggs. In the experiment illustrated in Fig. 1, no eggs were penetrated by incubation of sperm in medium 199 M for up to 10 h. After 4 h in 199 M there was a noticeable decline in both the proportion of sperm which were motile and in their individual speed. This decline continued, until after 10 h in 199 M alone there remained very few motile sperm. After only 4 h in the presence of oviduct material were

sperm suspensions produced, which penetrated 76% of the ova added to them within 90 min. This proportion increased to a maximum of 88% after 5 h of incubation and then declined, until by 10 h only 5% of the eggs were penetrated. The initial active motility was maintained throughout the 10 h. Capacitation of the sperm occurred more slowly in β -glucuronidase than in the oviduct contents and required 8 h to reach a maximum (70% of the ova were penetrated) before declining. The enzyme seemed to be as effective as the oviduct material in maintaining active sperm motility, except that after 4 h there was a transient decline in sperm activity. This was restored by 6 h of incubation.

To establish the specificity of action of the β -glucuronidase preparation, the effect of the β -glucuronidase inhibitor, glucaro-(1 $\rightarrow$ 4)-lactone (Calbiochem)⁸, was investigated. Table 1 shows that this inhibitor blocked β -glucuronidase capacitation completely, but did not interfere with the capacitation induced by the contents of the oviduct.

These experiments show that hamster sperm are capacitated *in vitro* by β -glucuronidase, but we conclude that this is not the mechanism by which capacitation is achieved by the oviduct contents, or *in vivo*. Capacitation by β -glucuronidase indicates, for the first time, that conjugated glucuronides form a component of the mammalian sperm surface. Presumably such glucuronides are components of glycoproteins or glycolipids which could also be hydrolysed enzymatically at other points in their structure. Such enzymatic hydrolysis may be the method of capacitation within the female genital tract. So far we have investigated only a limited number of possible candidates, but we can say that the enzyme β -amylase, reported by Kirton and Hafs several years ago to capacitate rabbit sperm⁹, and also α -amylase, trypsin and α -chymotrypsin do not capacitate hamster sperm. β -Glucuronidase is not required during the penetration period, for in our unpublished experiments, β -glucuronidase-capacitated sperm after centrifuge-washing still entered eggs within 90 min. There was no evidence for low molecular weight factors, other than those provided by medium 199 M; exhaustive dialysis of β -glucuronidase solutions did not reduce their effectiveness for capacitation.

R. B. L. GWATKIN

C. F. HUTCHISON

Merck Institute for Therapeutic Research,
Rahway, New Jersey

Received November 23, 1970.

¹ Barros, C., and Austin, C. R., *Anat. Res.*, **157**, 209 (1967).

² Yanagimachi, R., *J. Reprod. Fert.*, **18**, 275 (1969).

³ Gwatkin, R. B. L., and Andersen, O. F., *Nature*, **224**, 1111 (1969).

⁴ Yanagimachi, R., *J. Exp. Zool.*, **170**, 269 (1969).

⁵ Lobel, B. L., Rosenbaum, R. M., and Deane, H. W., *Endocrinology*, **68**, 232 (1961).

⁶ Hyashi, M., *J. Histochem. Cytochem.*, **12**, 659 (1964).

⁷ Gwatkin, R. B. L., and Williams, D. T., *Nature*, **227**, 182 (1970).

⁸ Levvy, G. A., *Biochem. J.*, **52**, 464 (1952).

⁹ Kirton, K. T., and Hafs, H. D., *Science*, **150**, 618 (1965).

Table 1 Effect of Glucaro-(1 $\rightarrow$ 4)-lactone (GL) on Capacitation of Sperm by β -Glucuronidase and Oviduct Contents

Treatment of sperm	Proportion of ova with zona penetrated by sperm
β -Glucuronidase, 20 μ g/ml.	14/26 (54%)
" " + GL, 5 μ g/ml.	0/30 (0%)
Oviduct contents	11/20 (55%)
" " + GL, 5 μ g/ml.	23/26 (90%)
" " + GL, 25 μ g/ml.	14/14 (100%)

Absence of Adrenergic Nerves in the Human Placenta

ALTHOUGH it is generally accepted that nervous tissue is absent in the human placenta and umbilical cord¹, the presence or absence of nerves has long been a controversy. In a review of the literature to 1943, Spivack² surveyed the reports of an innervation, which was variously described as adrenergic, cholinergic, myelinated, non-myelinated and a diffuse anastomosing network. Spivack, however, pointed out the difficulties of interpreting results with conventional neurological stains and described work with silver and methylene blue staining which gave no evidence of a nervous apparatus. There have been several recent reports of neuronal components in these tissues^{3,5}. Jacobson *et al.*^{6,7} presented evidence of nerves in

the placenta of human and other primate species. Using a modified methylene blue technique^{8,9}, they suggested that this innervation was intrinsic, with groups of cell bodies within the placenta, nerve bundles in the villi and fine fibres about vessels.

Modern histochemical techniques have not demonstrated adrenergic or cholinergic nerves in the human umbilical cord¹⁰. Using the sensitive Falck-Hillarp method, Ehinger *et al.*¹⁰ could only find catecholamine fluorescence in pre-terminal nerve bundles which ended blindly 1 cm into the cord from the foetus, with no evidence of terminal adrenergic fibres extending down the cord.

We have excised specimens of human umbilical cord, placental artery and vein from the chorionic plate (approximately 1 cm long) and small pieces of tissue (approximately 1 cm³) from the chorionic stem within 3 min of delivery, and incubated them in a solution of α -methyl noradrenaline (5×10^{-6} g/ml.: in Krebs Ringer) for 30 min at 37° C. This technique has been used with other foetal tissue to increase the sensitivity of this histochemical technique by allowing uptake of the monoamine oxidase-resistant α -methyl noradrenaline into nerves containing subthreshold concentrations of noradrenaline¹¹. By this procedure it is possible to identify adrenergic structures in situations where neuronal catecholamines are low or depleted. After incubation, the tissues were rinsed in fresh Krebs solution to remove excess α -methyl noradrenaline, quenched in liquid propane (-185° C), freeze-dried and incubated in formaldehyde vapour for 1 h at 80° C following the procedure described before¹². Paraffin sections (10 μ m) were then viewed for catecholamine fluorescence.

Fluorescence microscopy of specimens from eleven placentae failed to reveal specific catecholamine fluorescence in neuronal structures related to blood vessels or within extravascular tissue. The walls of the umbilical and placental arteries exhibited an increased fluorescence after incubation, due to the uptake of α -methyl noradrenaline by the smooth muscle cells. These non-innervated smooth muscle cells have an extremely low threshold for uptake of noradrenaline¹³, which may be related to the lack of adrenergic innervation.

We have been unable to detect an adrenergic innervation of the human placenta and umbilical cord at term even with incubation in α -methyl noradrenaline. No evidence was found of terminal fibres running down the cord or of an intrinsic innervation of the placenta. It remains possible that the nerves reported by Jacobson *et al.*^{6,7} are cholinergic, especially as it has been suggested that methylene blue has a greater affinity for cholinergic nerves¹⁴. While the intrinsic innervation reported by Jacobson *et al.*^{6,7} may have a different functional nature, ultrastructural studies have failed to find evidence for the presence of nerves either as bundles or as perivascular nets in the human placenta¹⁵. This suggests that the elements stained by Jacobson *et al.*^{6,7} are non-neuronal.

This work was supported by grants to Professor G. Burnstock from the Australian Research Grants Committee and the National Heart Foundation of Australia.

DAVID W. WALKER

Department of Obstetrics and Gynaecology,
Monash University,
Melbourne

JOHN R. McLEAN

Department of Zoology,
University of Melbourne,
Parkville 3052

Received October 26, 1970.

¹ Bourne, G., *The Human Amnion and Chorion*, 276 (Lloyd-Luke, London, 1962).

² Spivack, M., *Anat. Rec.*, **85** (1943).

³ Coujard, R., Lapage, F., and Schramm, B., *Bull. Fed. Soc. Gynec. et d'Obstet.*, Suppl. 4, 522 (1952).

⁴ Kernbakh, M., *Akush. Iginek.*, **5**, 15 (1959).

⁵ ten Berge, B. S., *Gynecologia*, **156**, 49 (1963).

⁶ Jacobson, H. N., and Chapler, F. K., *Nature*, **214**, 103 (1967).

⁷ Fox, H., and Jacobson, H. N., *Acta Anat.*, **73**, 48 (1969).

⁸ Miller, M. R., and Kasahara, M., *Anat. Rec.*, **145**, 13 (1963).

⁹ Hillarp, N.-Å., *Acta Physiol. Scand.*, **46**, Suppl. 157 (1959).

¹⁰ Ehinger, B., Gennser, G., Owman, Ch., Persson, H., and Sjöberg, N.-O., *Acta Physiol. Scand.*, **72**, 15 (1968).

¹¹ Read, J. B., and Burnstock, G., *Histochemie*, **20**, 197 (1970).

¹² Nakanishi, H., McLean, J., Wood, C., and Burnstock, G., *J. Reprod. Med.*, **2**, 20 (1969).

¹³ Burnstock, G., McLean, J. R., and Wright, Mary, *Brit. J. Pharmacol.* (in the press).

¹⁴ Ehinger, B., Sporrang, B., and Stenevi, U., *Histochemie*, **13**, 105 (1968).

¹⁵ Boyd, J. D., and Hamilton, W. J., *The Human Placenta*, 217 (Heffer, Cambridge, 1970).

Induction of Acetylcholinesterase Activity in Mouse Neuroblastoma Tissue Culture Cells

Tissue culture cell lines of neuroblastoma cells derived from mouse tumours have many characteristics of sympathetic neurones. Cells grown on a solid surface elaborate long processes which resemble axons^{1,2}, and they contain the enzymes of catecholamine synthesis as well as acetylcholinesterase and choline acetylase^{1,2}.

Shortly after obtaining a clonal line of these cells, we observed that few cells in a growing culture possessed axon-like extensions. Reasoning that the process of cell division, and particularly of mitosis, might antagonize the expression of the differentiated morphology, we examined the effect of stopping cell growth on the extension of processes by the cells. Removal of the calf serum from the culture medium was quickly followed by the formation of axon-like processes by nearly all cells, as observed by others³. We have also observed that stopping cell growth with inhibitors of DNA synthesis has similar effects to those of serum withdrawal. Both fluorodeoxyuridine (FUDR) and cytosine arabinoside (CAR), which arrest cells at the beginning of the S phase of the cell cycle, promote extensive elaboration of axon-like processes, but the drugs are less suitable than serum removal because the cells tend to die after exposure to the drugs for several days.

In view of the dramatic effects of stopping cell proliferation, we have investigated the effects on the levels of activity of certain enzymes of importance in neurotransmission.

The mouse neuroblastoma tissue culture line was derived from a clone NB42B isolated by Augusti-Tocco¹ and was a gift from Gordon Sato of the University of California, San Diego. Cells were grown in Falcon plastic culture bottles in Eagle's minimal medium⁴ supplemented with 10% calf serum.

Cells used for experiments were plated on plastic Petri dishes and allowed to grow for 2 days, when the medium was removed and serum-free medium was added.

Cell extracts were obtained from cells removed from the Petri dishes, with versene solution, washed with phosphate-buffered saline, resuspended into 0.01 M Tris-HCl buffer, pH 7.5, and then sonicated for 15 s with an MSE instrument at 8 μ m amplitude.

Acetylcholinesterase was assayed with the crude sonicate of neuroblastoma cells after treatment of the latter with 'Triton-X100' (final concentration, 0.5%), according to the method of Ellman⁵. Small amounts of butyrylthiocholine hydrolysed by nonspecific esterases were always subtracted from the larger amounts of acetylthiocholine hydrolysed, to give a specific measure of acetylcholinesterase activity. Tyrosine hydroxylase activity was assayed by the method of Levitt *et al.*⁶, except that 3H-tyrosine was purified on 'Dowex-50-H⁺' just before use. The sonicated cell extract was used directly in this assay. Choline acetylase was assayed with the sonicate after treatment with 'Triton-X100' (final concentration, 0.5%) as described by Potter *et al.*⁷. Neurotubule protein was assayed by the radioactive colchicine binding assay of Borisy and

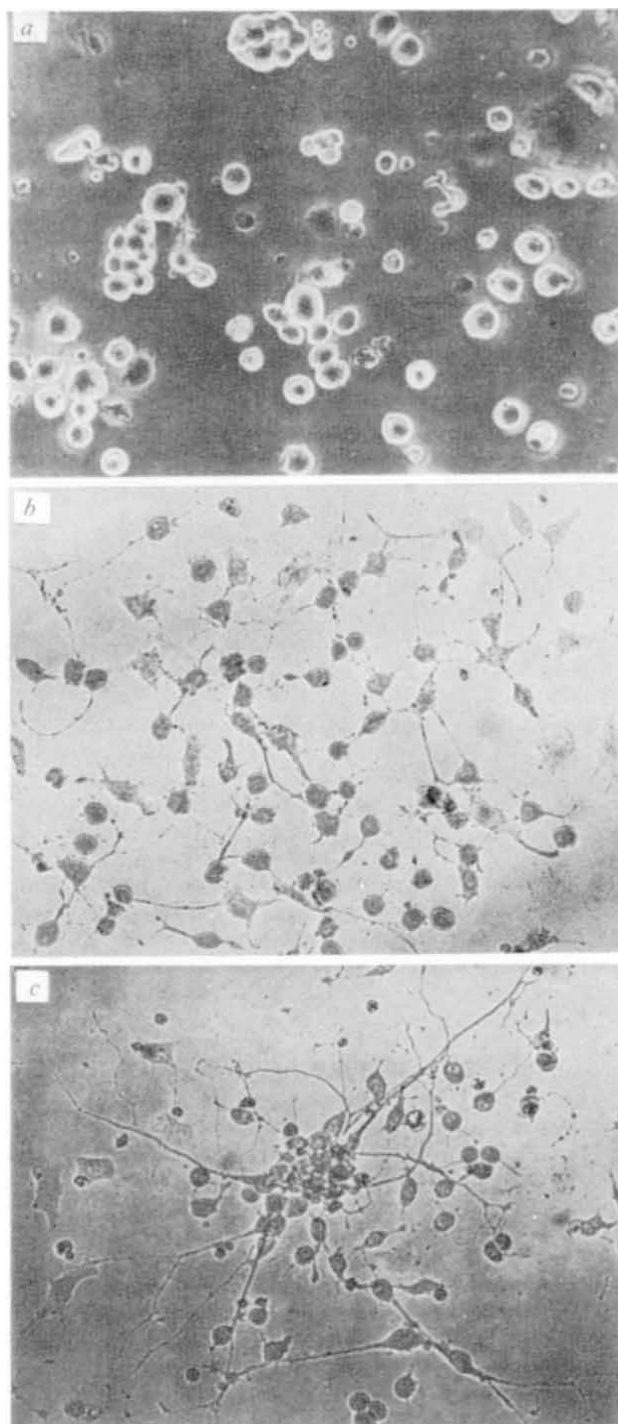


Fig. 1 Morphology of growing and non-growing neuroblastoma cells in culture. *a*, Logarithmically growing culture; *b*, cells 3 days after removal of serum from the culture medium; *c*, 5 days after removal of serum.

Taylor⁸ using the soluble protein fraction from cells sonicated in 0.01 M Tris, pH 7.0, containing 1×10^{-3} M $MgCl_2$ and 0.25 M sucrose.

Fig. 1 shows the immunological difference between growing and non-growing, serum-free cultures of our neuroblastoma cell line (compare the results of Seeds *et al.*³).

Increases in specific activity of acetylcholinesterase after removal of serum from the culture medium (Fig. 2) are nearly completely inhibited by actinomycin D (0.1 $\mu g/ml.$) and cyclohexamide (10 $\mu g/ml.$), suggesting that *de novo* protein and RNA synthesis is required for the increase in activity. These two drugs have little effect on the elaboration of axon-like processes by the cells in the first 36 h of culture in serum-free medium, which agrees with previous findings³. Even in con-

centrations five times lower than those which we used, these two drugs cause neuroblastoma cells to lyse after 48 h. Our findings on drug inhibition of enzyme induction should therefore be viewed with reservations.

Because the arresting of cellular DNA synthesis by FUdR and CAR causes generalized elaboration of axon-like extensions in a neuroblastoma culture, we have tested the effect of these drugs on acetylcholinesterase activity in cells maintained in the presence of serum. Table 1 indicates that enzyme activity increases after one addition of these drugs to the level reached after removal of serum. Thus there seems to be nothing in serum which directly antagonizes the increase in acetylcholinesterase activity.

Table 1 Induction of Acetylcholinesterase by Inhibitors of Cellular DNA Synthesis

Medium	Relative specific activity acetylcholinesterase
Complete	1
Complete+FUdR	5.1
Complete+CAR	4.8
Serum-free	5.7

Acetylcholinesterase activity was measured 24 h after addition of the drugs or the removal of serum from the culture medium. Both fluorodeoxyuridine (FUdR) and cytosine arabinoside (CAR) were present at a concentration of 10^{-5} M (1×10^{-4} M uridine was added along with the FUdR).

Table 2 Lack of Induction of Other Neurone Proteins

Protein	Relative specific activity			
	0 h	24 h	48 h	72 h
Tyrosine hydroxylase	1.0	1.5	2.0	1.0
Choline acetylase	1.0	1.0	2.7	1.9
Neurotubule	1.0	1.0	0.75	—
Acetylcholinesterase	1.0	5.7	23	22

The specific activity relative to total cellular protein of several neural proteins in neuroblastoma cells is shown as a function of time after removal of serum from the cellular culture medium.

Table 2 indicates that the concentrations of choline acetylase, tyrosine hydroxylase and neurotubule protein do not increase when cell growth is arrested by the withdrawal of serum.

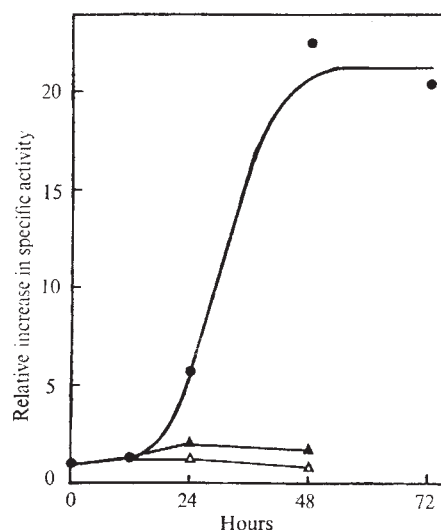


Fig. 2 Increase in specific activity of acetylcholinesterase after removal of serum from the culture medium of mouse neuroblastoma cells. Cell cultures in logarithmic growth were transferred to serum-free medium at time zero on the abscissa. Cell extracts were assayed for acetylcholinesterase activity as described in the text. Generally about 1 μmol of acetylthiocholine was hydrolysed per mg protein/min in non-induced cells. ●, No drugs; ▲, 0.1 $\mu g/ml.$ of actinomycin D added; △, 10 $\mu g/ml.$ of cyclohexamide added.

Thus the increase in acetylcholinesterase seems to be somewhat specific. The absence of increase in neurotubule protein is consistent with the earlier results³, showing that protein synthesis is not required for initial elaboration of processes after removal of serum, implying that pre-existing neurotubule protein can be utilized.

We have observed, in agreement with the results of Seeds *et al.*³, that transfer of neuroblastoma cells to serum-free medium induces most cells in the culture to elaborate axon-like processes. We also found that the latter processes are formed to the same extent if drugs which inhibit cellular DNA synthesis are added to the cells, even in the presence of serum. This indicates that serum *per se* does not inhibit the extension of axons directly, but probably acts by promoting cell growth and division which is antagonistic to morphological differentiation. For example, time lapse cinematography has shown that mitotic neuroblastoma cells withdraw their axon-like extensions completely (unpublished observations).

The fact that we observed a sizable induction of an enzyme involved in neural transmission accompanying the morphological differentiation suggests that a rather complex differentiation process may occur as a result of stopping cell proliferation. Not all enzymes involved with neural function were observed to increase, however. The drug studies suggest that there is *de novo* enzyme synthesis. It is conceivable that acetylcholinesterase is normally synthesized in the late G₁ phase of the cell cycle. Then the induction observed after removal of serum and addition of drugs could be accounted for by an arrest of the cells in late G₁ and early S, and cholinesterase synthesis would continue for extended periods in these non-growing cells.

This work was supported in part by grants from the US Public Health Service, National Institute of Mental Health, National Institute of Allergy and Infectious Diseases and National Institute of General Medical Sciences.

JOSEPH R. KATES
RADENE WINTERTON
KURT SCHLESSINGER

Departments of Chemistry and Psychology,
University of Colorado,
Boulder, Colorado 80302

Received July 30; revised September 1, 1970.

- ¹ Augusti-Tocco, G., and Sato, G., *Proc. US Nat. Acad. Sci.*, **64**, 311 (1969).
- ² Schubert, D., Humphreys, S., Baroni, C., and Cohn, M., *Proc. US Nat. Acad. Sci.*, **64**, 316 (1969).
- ³ Seeds, N. W., Gilman, A. G., Amano, T., and Nierenberg, M. W., *Proc. US Nat. Acad. Sci.*, **66**, 160 (1970).
- ⁴ Eagle, H., *Science*, **122**, 501 (1955).
- ⁵ Ellman, J. L., Courtney, K. D., Andres, jun., V., and Featherstone, R. M., *Biochem. Pharmacol.*, **1**, 88 (1961).
- ⁶ Levitt, M., Gibb, J. W., Daly, J. W., Lipton, M., and Udenfriend, S., *Biochem. Pharmacol.*, **16**, 1313 (1967).
- ⁷ Potter, L. T., Glover, V. A. S., and Saelens, J. K., *J. Biol. Chem.*, **243**, 3864 (1968).
- ⁸ Borisy, G. G., and Taylor, E. W., *J. Cell. Biol.*, **34**, 525 (1967).

Effects of LSD on Receptive Fields of Single Cells in the Lateral Geniculate Nucleus of the Cat

SMALL doses (~100 µg) of lysergic acid diethylamide (LSD) taken orally cause hallucinations and distortions of visual perception in man¹. The latter effects suggest that LSD disturbs normal integrative functions in the visual pathways. It is known that transmission through the visual pathways is depressed by the drug, for small doses (15–30 µg/kg) given parenterally depress the response of the cat lateral geniculate nucleus (LGN) to shocks applied to the optic nerve^{2,3}. Similar doses have no effect on the responses of the visual cortex to electrical stimulation of the optic radiation. These results

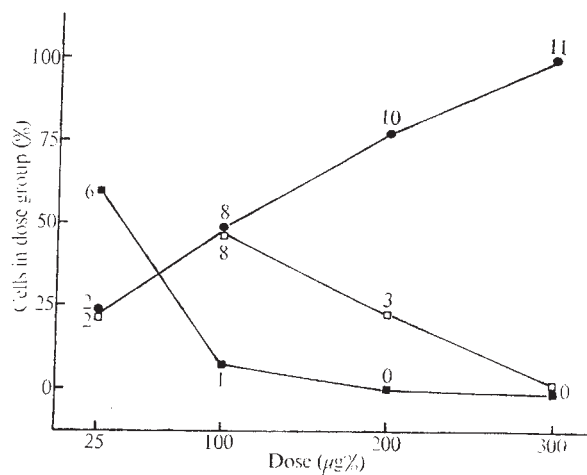


Fig. 1 Effects of LSD on spontaneous activity. Percentage of cells in which spontaneous activity was reduced by LSD (●); increased by LSD (□), and unchanged (■). The number of cells is shown beside each point. The number of cells of which activity was depressed is significantly greater for the higher doses (200 µg, $P < 0.05$; 300 µg, $P < 0.01$) than when the dose was 25 µg. Each cat weighed 3 kg.

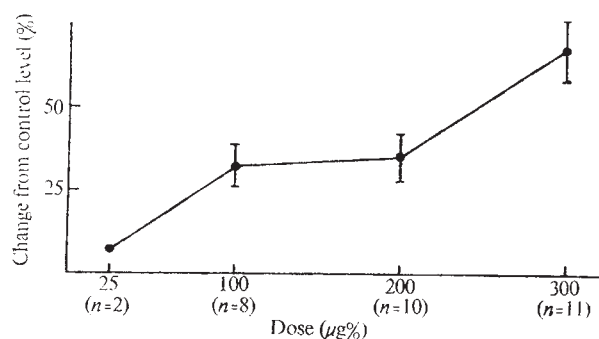


Fig. 2 Percentage reduction in mean spontaneous firing rate (ordinate) of cells depressed by LSD, in relation to dose (abscissa). Each point on the graph shows the average mean decrease in firing rate for each dose. The number of cells (*n*) in each dose level is given below the abscissa. The vertical bars show the standard errors. No standard error is shown for the 25 µg group because only two cells in this group were inhibited. Each cat weighed 3 kg.

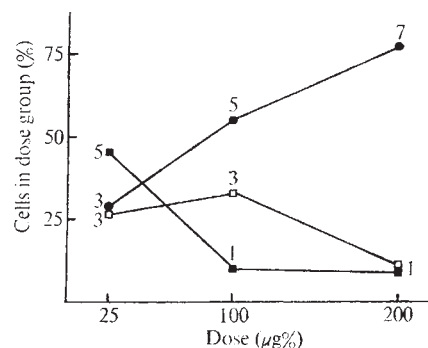
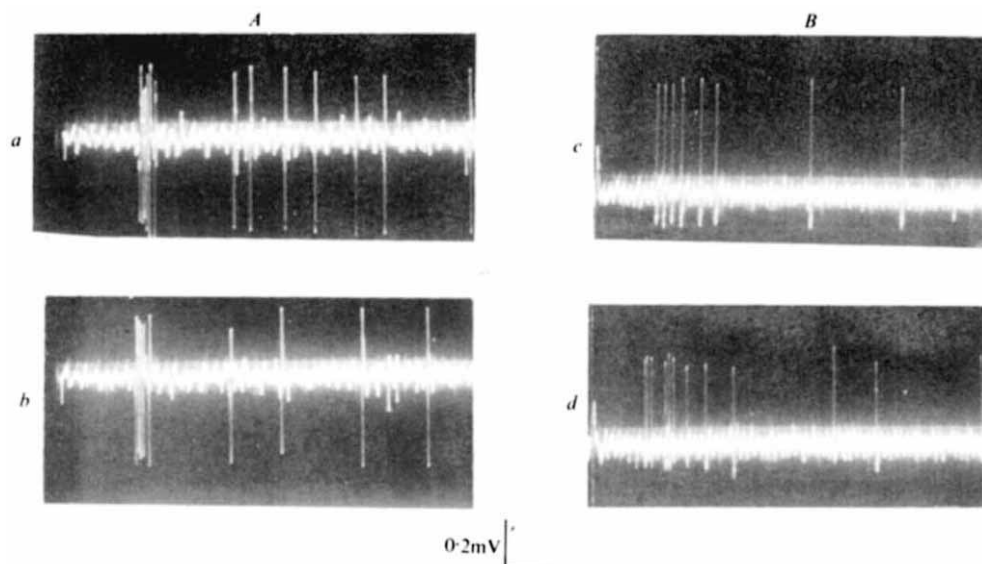


Fig. 3 Effects of LSD on the light-evoked responses of field centres of LGN cells. The number of cells is shown at each point. Symbols are as in Fig. 1. Each cat weighed 3 kg.

suggest a relatively selective influence of LSD on the LGN, which is known to be involved in the integration of signals passing to the visual cortex from the optic tract⁴. This function can be analysed by studying the receptive fields of single cells in the nucleus. We have therefore studied the effects of LSD on the spontaneous and evoked activity of cells in the LGN of cats, and present a brief account of some of our findings.

Sixteen adult cats (mean weight 2.7 ± 0.33 (s.d.) kg) were used. Anaesthetic and surgical techniques were similar to those described earlier, as were the methods for recording from single

Fig. 4 Responses of two LGN units to light shone on the centres of their receptive fields. *A*, Cell with "on" centre, "off" surround. Centre responses before (*a*) and after (*b*) 100 μ g of LSD had been administered. Analysis of the data for this cell showed that the centre responses were significantly ($P < 0.002$) smaller after the drug had been given than before. Trace triggered by onset of light. *B*, Cell with "off" centre, "on" surround. Centre responses before (*c*) and after (*d*) 100 μ g of LSD. Responses significantly ($P < 0.002$) larger after injection than before. Responses *b* and *d* were recorded about 5 min after the injection of LSD. Time scale was 36 ms for *a* and *b* and 50 ms for *c* and *d*.



cells and plotting receptive fields⁵. In all experiments, background luminance was 4 cd m⁻². After the field of an LGN cell had been plotted, a spot of light was focused on the centre of the field. The spot, which lasted 0.5 s and was 1.5 to 2 log units brighter than background luminance, was presented twenty times at 5 s intervals. The surround region of the field was similarly stimulated, but by an annulus of light. These responses and also the spontaneous activity of the cell were recorded on magnetic tape (control data). A dose of LSD (hydrogen tartrate salt), dissolved in 0.5 ml. of normal saline, was then injected through a cannula in the saphenous vein. The dose was 25, 100, 200, or 300 μ g, each approximating to 10, 40, 80 and 120 μ g/kg. Immediately after the injection the spontaneous activity and then the responses (experimental data) of the centre and surround of the field were recorded. Control and experimental data were compared. The period (3 min) in which spontaneous activity was recorded was broken down into epochs of 10 s. The number of spikes in each epoch was counted. Control and experimental counts were compared using the Mann-Whitney *U* test (two-tailed) and were considered significantly different if $P < 0.05$. The number of spikes present in the 0.5 s after the onset ("on" responses) or offset ("off" responses) of the light was counted for each set of twenty stimuli. Data for control and experimental responses were compared as described for spontaneous activity. Fifty cells were studied and data on field plots were obtained from twenty-nine of them. All statistical tests are two-tailed except where stated.

LSD affected spontaneous activity in a dose-dependent manner within a few seconds of the injection (Fig. 1). The percentage of cells of which spontaneous activity was reduced increased with the dose. The mean reduction in firing rate, expressed as a percentage of the mean control value, was greatest (68.3 ± 8.8 s.e.) with the largest dose (Fig. 2): the depression of activity was greater ($P < 0.05$) for this dose than for doses of 100 or 200 μ g, for which the percentage changes do not differ significantly.

Not all the effects observed were depressive (Fig. 1). The spontaneous activity of eight out of seventeen cells was increased after injection of 100 μ g of LSD, but was not increased in any of the eleven cells in the 300 μ g sample. This difference was significant ($P < 0.01$). The facilitatory effect of the 100 μ g dose was often considerable and amounted to a mean percentage increase in firing rate of 65.1 ± 21.4 (s.e.), compared with the pre-injection rate.

The effects on spontaneous activity of ≥ 200 μ g of LSD suggested that such doses would depress the evoked discharges to photic stimulation, an expectation which is supported by the data in Fig. 3. This graph is derived from a study of the centre responses of twenty-nine cells. When 25 μ g of LSD was given,

the responses of only three out of a sample of eleven cells were reduced. When 200 μ g was given, the responses of seven out of nine cells were reduced. These proportions were significantly ($P < 0.05$, 1 tailed) different. An example of a unit of which centre response was depressed is shown in Fig. 4 *a* and *b*.

With all three doses used in the experiments on which Fig. 3 is based, the responses of some cells to centre (and also to surround) stimulation were significantly increased. Data for a unit with a centre response which was increased are shown in Fig. 4 *c* and *d*. Doses of ≤ 100 μ g were less depressive than a dose of 200 μ g.

In fourteen out of twenty-six cells the responses to centre and surround stimulation were both affected by LSD in the same direction (that is the responses were either both decreased or both increased). In the other twelve cells the effects on the centre and surround responses were not in the same direction. There was no consistent relationship between field type ("on" centre or "off" centre) and the influence of LSD. Mixed effects of the drug on the centre/surround organization were more common when doses of ≤ 100 μ g were given than when the dose was 200 μ g. Thus the centres and surrounds of seven of the nine cells in the group receiving 200 μ g of LSD were affected in the same way (all depressed), whereas the centres and surrounds of only two of the eleven cells in the group receiving 25 μ g were similarly affected. These proportions are significantly different ($P < 0.02$).

In doses of ≥ 200 μ g, LSD tends to depress the spontaneous and evoked activity of cells in the LGN, a result which is consistent with the observation that very large (1 mg/kg) doses of LSD given to unanaesthetized cats cause blindness, which is reversible³. Lower doses affect the organization of the receptive fields in the LGN in a complex way. Frequently, there is a change in the normal balance of centre/surround antagonism. This antagonism is thought to be an important mechanism for sensory contrast^{6,7}, and is almost certainly connected with pattern discrimination in the visual cortex⁸: so interference with the normal balance of this antagonism is likely to influence these functions. It is interesting that the lower doses used in these experiments were in the same range as that which, in man, is known to result in complex visual disturbances.

We thank the Nuffield Foundation for financial support, Sandoz Pharmaceuticals for LSD, and Dr R. M. Marchbanks and Mr B. R. Slater for their help.

JENNIFER M. MCKAY
GABRIEL HORN

Department of Anatomy,
University of Cambridge.

Received June 23; revised September 11, 1970.

- ¹ Hoffer, A., and Osmond, H., *The Hallucinogens* (Academic Press, New York and London, 1967).
- ² Evarts, E. V., Landau, W., Freygang, W., and Marshall, W. H., *Amer. J. Physiol.*, **182**, 594 (1955).
- ³ Bishop, P. O., Field, G., Hennesy, B. L., and Smith, J. R., *J. Neurophysiol.*, **21**, 529 (1958).
- ⁴ Hubel, D. H., and Wiesel, T. N., *J. Physiol.*, **155**, 385 (1961).
- ⁵ Horn, G., and Hill, R. M., *Nature*, **221**, 186 (1969).
- ⁶ Barlow, H. B., in *Sensory Communication* (edit. by Rosenblith) (MIT Press and Wiley, New York and London, 1961).
- ⁷ Horn, G., in *Viewpoints in Biology* (edit. by Carthy and Duddington), **1** (Butterworths, London, 1962).
- ⁸ Hubel, D. H., and Wiesel, T. N., *J. Physiol.*, **160**, 106 (1962).

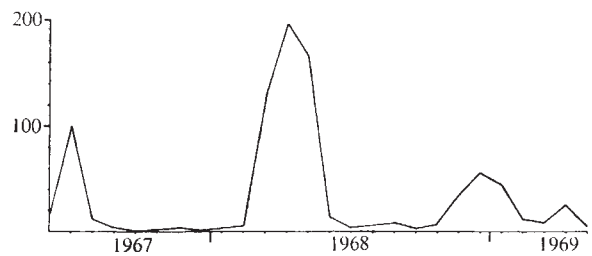


Fig. 2 Numbers of young *Agriolimax reticulatus*, weighing less than 25 mg, from soil samples.

The Leap-frogging Slug

PREVIOUS reports of the life cycle of the slug, *Agriolimax reticulatus* (Müller)¹⁻⁴, have maintained that there are two generations a year. A spring generation hatches in March to May and grows during the summer to give rise to an autumn generation which hatches in September to October and this grows during the winter to produce the next spring generation. In a recent study at Cambridge this pattern seemed to be confirmed. Outdoor cultures of *A. reticulatus* were kept on soil with adequate food and moisture and laid eggs within 5-7 months of hatching.

A field sampling study at the same time showed, however, that this pattern may not always be followed. Slugs in their natural environment do not always have adequate food and moisture so that their growth is slower. Moreover, the development time of their eggs can be considerable, particularly during the winter months, when *A. reticulatus* takes more than 3 months to hatch (Table 1). When these factors are taken into account, two complete generations a year would not always be possible.

Table 1 Mean Time taken by Egg Batches, kept Out of Doors, to Hatch

Period of egg deposition	No. of batches	Mean weeks to hatch
1 10 68-14 10 68	7	4
15 10 68-28 10 68	12	5
29 10 68-11 11 68	5	8
26 11 68- 9 12 68	5	12
10 12 68-23 12 68	4	13
24 12 68- 6 1 69	3	14
7 1 69-20 1 69	3	13
21 1 69- 3 2 69	1	12
4 2 69-17 2 69	1	11
18 2 69- 3 3 69	3	10
4 3 69-17 3 69	3	9
18 3 69-31 3 69	1	7
15 4 69-28 4 69	3	5
29 4 69-12 5 69	7	5
13 5 69-26 5 69	5	4

The field samples were taken every 4 weeks from an uncultivated plot near Cambridge. Twelve sampling units, each of 1 cubic foot of soil, were dug every 4 weeks and the slugs extracted from this soil by flooding³. The slugs were weighed, dissected and examined for maturity. The weights were divided into 50 mg categories and analysed by the method of

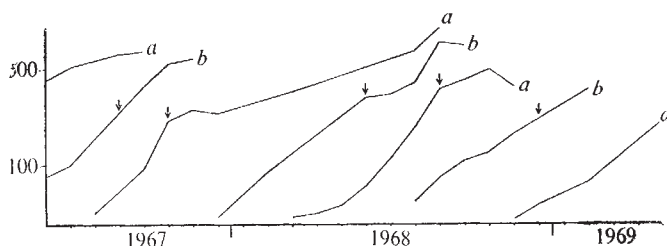


Fig. 1 Growth rates of *Agriolimax reticulatus* in a natural population. The arrow indicates the first appearance of mature slugs in each generation.

Harding (1947) (ref. 2). By this method, it is possible to separate superimposed frequency distributions representing individual generations (Fig. 1). From this analysis, there seemed to be several overlapping generations at certain times of the year.

In general, there seemed to be two "leap-frogging" sets of generations: (a) a generation hatching in July 1967 giving rise to a generation in April 1968, which in turn produced a generation in December 1968 (Fig. 1a); and (b) a slug generation hatching in November 1967; this produced a small generation in August 1968 which in turn gave rise to a generation in April 1969 (Fig. 1b). This conclusion was confirmed when the numbers of newly hatched *A. reticulatus* in samples were considered separately (Fig. 2). Each peak in numbers of these slugs coincided with the appearance of a new generation so demonstrated above. Although this preliminary work demonstrates the possible basic pattern of the *A. reticulatus* life cycle, variation may occur in other years and in other regions. Also, there is probably considerable variation within each generation itself: some slugs may mature quickly enough to contribute to the generation immediately following it, as well as their main contribution to the next but one generation. Although many soil dwelling invertebrates have overlapping generations, it is unusual for an invertebrate to have a "leap-frogging" generation pattern like this, particularly when the generation interval is of 9 months.

A knowledge of the biology and ecology of these crop pests will be vital to their efficient control: many control systems are at present designed to reduce populations immediately before the breeding season and it may now be necessary to modify these systems.

We thank Miss L. Hazlewood and Mr S. C. O'Donohue for assistance in the laboratory and field. This work was supported by an Agricultural Research Council special grant.

P. J. HUNTER

International Scientific Relations Division,
Department of Education and Science,
Africa House,
Kingsway, London WC2B 6BD

B. V. SYMONDS

National Agricultural Advisory Service,
Brooklands Avenue, Cambridge

Received February 19; revised October 22, 1970.

¹ Bett, J. A., *Proc. Zool. Soc. Lond.*, **135**, 559 (1960).

² Harding, J. P., *J. Mar. Biol. Assoc.*, **28**, 141 (1947).

³ Hunter, P. J., *Malacologia*, **6**, 379 (1968).

⁴ Hunter, P. J., *Malacologia*, **6**, 369 (1968).

Extensions to the Study of Science Students' Divergent Thinking Ability

AN important aspect of creative performance in several fields of endeavour is the ready production of diverse ideas. Several paper and pencil tests have been devised to measure the

ability to produce quickly a large number of ideas within the limits set by the test instructions. If the scoring procedure emphasizes the number rather than the quality of appropriate responses within a time limit, the resulting score is said to measure "fluency of divergent production".

In a previous experiment, groups of university arts students obtained higher fluency scores than science students, using the "unusual uses" and the "similarities" tests¹. Similarly, Hudson has reported that pupils studying arts subjects in the senior forms of British secondary schools score higher on divergent thinking tests than those studying science², and this finding has been replicated in Australian schools³.

The reason for the poorer performance of science students is not that they are generally less intelligent. Several studies suggest that science students perform well with reasoning or numerical problems which require convergent thinking towards a single correct solution^{4,5}. Moreover, there is little correlation between conventional intelligence quotient (IQ) and divergent thinking scores with university samples; for example, an approximately zero correlation was found in a sample of 100 students of the University of Adelaide⁶. The lower scores of science students specifically on divergent thinking tests are of concern, because the creativity of "research and development" scientists seems to be related to their divergent thinking ability^{7,8}.

It could be argued, however, that divergent thinking tests are biased against science students because of their interests and attitudes. In particular, many tests are concerned with word usage, and science students sometimes give a relatively poor performance on tests with verbal rather than numerical or spatial material. Therefore, both a verbal battery and a non-verbal battery were used in the experiment to be described here.

It could also be argued that the science student obtains low fluency scores because he is less likely to interpret the standard instructions of divergent thinking tests as allowing improbable or whimsical responses. If this were so, the difference between arts and science students should be reduced with more permissive instructions. To investigate this possibility, different groups of subjects were given one of three kinds of written instruction. The "standard" instruction required the subject to give as many responses as he could. The "more permissive" instruction included the additional sentence: "Please give any response at all that occurs to you". The "most permissive" instruction had the additional phrase: "no matter how far fetched it may appear to you".

These instructions were given to three separate groups of male students taking the course known as psychology I in the faculty of arts at the University of Adelaide. Three groups of male students taking engineering I in the faculty of engineering were similarly tested. There were twenty-two subjects in each of the six experimental groups so formed. A preliminary testing session with other subjects was used to improve the administration of tests. All subjects were given the two test batteries: half the subjects in each group did the verbal battery first, and half did the non-verbal battery first.

Both batteries consisted of four different tests, with three items in each. The time allowed for each test was 7.5 min, with a 5 min break between batteries. The tests used were similar to those in the ETS kit of reference tests for cognitive factors⁹ and in the Purdue creativity test¹⁰, but modified to suit the desired format.

The verbal battery consisted of listing words with given prefixes (for example "per"), questions (for example about "a cardboard box"), similes (for example for "dark") and consequences (for example if "all laws have been repealed"). The non-verbal battery consisted of listing objects which could be represented by given shapes, objects made from given materials (for example "glass"), purposes for which objects illustrated could be used, and objects fitting given descriptions (for example "long and thin"). These latter tests required written answers, but were non-verbal in the

sense that they referred to the properties of shapes and objects. It was considered that the content of the non-verbal tests would be more familiar to the engineering students, though not requiring specialized scientific knowledge.

Table 1 Mean Divergent Thinking (Fluency) Scores, for Arts and Engineering Students

Instructions	Arts	Faculty Engineering	Both
Means for verbal battery			
Standard	83.2	66.8	75.0
More permissive	92.7	80.9	86.8
Most permissive	106.3	84.0	95.2
Means for non-verbal battery			
Standard	94.5	62.2	78.3
More permissive	96.9	81.6	89.2
Most permissive	106.8	87.3	97.1

The score for each test was simply the number of responses which fitted the requirements of the test. Scores were summed to give a verbal and a non-verbal fluency score for each subject. The mean scores of the six groups are given in Table 1.

Differences between the means were tested for significance by two way analyses of variance. The principal effects of faculty and instruction were significant at the 1% level of confidence for both the verbal battery and the non-verbal battery. There was no significant interaction effect in either case. The results were therefore straightforward. The more permissive the instructions, the higher were the fluency scores, as expected. The arts students scored higher than the engineering students for each of the three types of instruction and for both test batteries. Moreover, the advantage of the arts students was not diminished with permissive instructions nor by the use of non-verbal tests. We conclude therefore that the poorer performance on divergent thinking tests of engineering students, and other groups of science students, is not limited to any particular test content or standard form of instruction.

If performance is so poor in spite of high intelligence, what motivates the convergent rather than divergent style of thinking among science students? One explanation is that convergers have learned to inhibit responses not conforming to the expectations of authority figures such as parents and teachers. It would be unfortunate if, in our efforts to teach pupils to conform to desirable standards of social behaviour, we also hindered the development of fluency with useful divergent ideas. Blade remarks¹¹: "Have we lost the creative and independent-minded students? Have we lost or not stimulated the student who would be challenged by open-ended problems rather than by closed-ended, single-answer problems . . . ?"

We thank the faculty of engineering at the University of Adelaide and in particular Devon Doble, a divergent thinker.

E. E. RUMP
MARGARET DUNN

Department of Psychology,
University of Adelaide

Received September 14; revised November 9, 1970.

¹ Rump, E. E., *Austral. NZ Assoc. Adv. Sci. Cong.*, Adelaide (1969).

² Hudson, L., *Contrary Imaginations* (Methuen, London, 1966).

³ Cropley, A. J., and Field, T. W., *Nature*, **217**, 1211 (1968).

⁴ Povey, R. M., *Brit. J. Psychol.*, **61**, 55 (1970).

⁵ Child, D., *Brit. J. Educ. Psychol.*, **39**, 40 (1969).

⁶ Rump, E. E., *Austral. Psychol. Soc. Conf.*, Brisbane (1968).

⁷ Jones, F. E., *J. Appl. Psychol.*, **48**, 134 (1964).

⁸ Shapiro, R. J., *Psychol. Africana*, Monog. Suppl. No. 4 (1968).

⁹ French, J. W., Ekstrom, R. B., and Price, L. A., *Manual for Kit of Reference Tests for Cognitive Factors* (ETS, Princeton, 1963).

¹⁰ Lawshe, C. H., and Harris, D. H., *Manual for the Purdue Creativity Test* (Purdue Foundation, 1960).

¹¹ Blade, M-F., in *Essays on Creativity in the Sciences* (edit. by Coler, M. A.) (New York University Press, 1963).

BOOK REVIEWS

Concepts of Order

Classical Scientific Papers: Chemistry. Second Series: Papers on the Nature and Arrangement of the Chemical Elements. Arranged and introduced by David M. Knight. Pp. xiii+441. (Mills and Boon: London; American Elsevier: New York, November 1970.) 100s; \$15.

THE *Classical Scientific Papers: Chemistry*—which I reviewed in 1968 (*Nature*, **218**, 605)—was not described as the first of a series, but, as I said then, it could not be left on its own. Dr Knight obviously knew how to pick papers of individual merit, how to put them together and how to present their significance and relation in a few stylish, sensible words of his own. He has done equally well in this second series, devoted to papers on the nature and arrangement of the chemical elements. The volume is intended primarily for English language readers, with only one short entry in French (Berthelot) and one in German (the abstract of Mendeléeff's first paper).

There are five sections, each chronological, but overlapping in period. The first, "The Rise and Fall of Prout's Hypothesis", establishes Knight's theme: that the search for an underlying unity in matter lay constantly at the back of all nineteenth century fundamental studies of matter from Prout himself to J. J. Thomson. Dr Knight argues that, as it stood in the early nineteenth century, the corpuscularian hypothesis was not susceptible to any direct quantitative test; the position was altered by Prout, when he adopted the Daltonian concept of atomic weights, put forward his concept of integral weights, and so laid the way open to the establishment of a prime matter of unit atomic weight. (The failure of this hypothesis in the face of analytical results which never threw up the kind of integral values Prout hoped for is not well illustrated in the texts because it was chiefly the detailed work of continental chemists, but this part of a long story cannot be told in a few striking papers.) The second section concerns an aspect of nineteenth century scientific thought which is little known but ought to appear very striking at the present time: theories of a fourth state of matter. It would be interesting to see what a philosopher of scientific ideas made of the apparent persistence of the ideas of

Faraday and Crookes in modern matter theory. The recent celebrations of the centenary of Mendeléeff's 1869 paper have emphasized the classification eventually reached, but the path to this peak has running alongside it constant reflexions on the composition of elements. There was an interesting interplay of ideas. Davy saw that as the ammonium radical behaved like an alkali metal, the alkali metals might themselves be compound. Later on, the phenomenon of organic isomerism suggested that a parallel phenomenon might exist in the elements: that although differing in properties, like isomers they were all compounds of some more elementary constituents. The development of the Periodic classification of the elements, achieved by modest men of modest pretensions, must surely rank as one of the great illuminations of the mind. Mendeléeff deserves his reputation. Dr Knight reprints a long serialized paper of 1879–80 which demonstrates all his grip and all his fluency. No wonder he was so welcome a visitor to England. The fifth group is headed "The Revival of Prout's Hypothesis". Is this really what Dr Knight means? None of the papers from Gladstone's of 1883 onwards really urges a naive Proutian theory, although the contribution of chemists to the eventual new theory of the atom is clear.

Most of the papers are theoretical or critical, but some are worth reading for their lessons in the interaction of one science with another and the interplay of theory and practice. Follow through, for example, Norman Lockyer's marvellous development of a line of enquiry into the origin of spectral lines, their meaning for a theory of atomic constitution, and the experimental programme demanded by unanswered questions. Crookes's patient fractionations of rare earths and his theory of "meta-elements" seem less marvellous because they ran into the sand, but none the less they are worth looking at because they were at least original in conception and expression.

The historian of science will value this collection for the stimulus it will give his own work. This sort of reprint, however, ought also to be read by research scientists, particularly young ones, as a corrective to the reading of modern scientific publications, with their soul-less

manner of presentation, which falsify the real scientific enquiry which lies behind them. These papers really say what people did and how they felt about it. They had not been subjected to dead-pan standardization either by institutional or publishing society editors; and they read like the work of live men, not of scientific battery hens. Perhaps *Nature* will hive off yet another section, in which authors will be able to write as they worked: worries, doubts, passions, rivalries and all getting across to the reader. In a hundred years' time papers like that would still be worth reprinting and reading for pleasure.

FRANK GREENAWAY

Stability and Change

Freedom in a Rocking Boat: Changing Values in an Unstable Society. By Geoffrey Vickers. Pp. 215. (Allen Lane, The Penguin Press: London, October 1970.) 50s.

THIS is the fourth of a series of books in which Sir Geoffrey Vickers is seeking to call on us to change our values and our priorities. This one concentrates on the need to reappraise the liberal-individualistic values of the western world in the face of the threat posed by the world's population explosion and by the consequences of technological change.

The discussion is conducted at several different levels, the economic, the political, the biological, even the religious, but the most powerful argument that Sir Geoffrey can present to his readers, and apparently the issue which weighed most heavily in his own mind, is the discovery of the ecological threat to the survival of humanity as a whole. Air and water pollution, the destruction of the ionosphere, the using up of oxygen faster than the plants can replace it—we do not know where the most fatal blow may fall, but sooner or later the anarchy of individual or national selfishness will bring about some great disaster unless humanity devises appropriate control mechanisms. Basically, the problem is not really as new as all that. Old-fashioned economists knew about "external diseconomies"—creating costs for others, for all in fact, that were not borne or considered by the firm making them. Old-fashioned socialism knew

about the need for social control to prevent the abuses of traditional "liberalism". The difference is, perhaps, that now that the threat is biological, it is not merely the poor or the weak who are in danger, but even the rich and the powerful; just as, a century ago, it was only when cholera and other diseases refused to stay in the poor quarters of the cities of Britain, but also threatened those in grand houses, that some elementary sanitary and social improvements were begun.

Of course, we need freedom within the world's social control. We also need flexibility, an acceptance of change, while preserving stability, that is, we require a system with control and feedback mechanisms which will keep it on its course while it is bombarded by new influences. We need to do all this while preserving the popular right to choose one's government, while maintaining free trade as far as possible, peace along the frontiers and prosperity even in the poor countries.

The book contains no blueprint for any of these, just hints, at best, on some of the most likely approaches. But at least the questions are the right ones, and the success with which Sir Geoffrey has overcome his own Victorian ideals to take account of changes in the world around him might serve as a model for men much younger than he.

SIDNEY POLLARD

Dating the Past

The Impact of the Natural Sciences on Archaeology. (A Joint Symposium of the Royal Society and the British Academy, organized by a committee under the chairmanship of T. E. Allibone, FRS.) Pp. vii + 185 + 3 plates. Published for the British Academy by Oxford University: London, January 1970.) 120s.

IN 1968, the officers of the Royal Society and the British Academy decided that, for the first time, these two bodies should work together in furthering knowledge in fields of common interest. The first fruit of this welcome decision was a joint symposium, and inevitably archaeology—the most obvious bridge subject between the natural sciences and the humanities—was selected as its subject. This handsome volume contains the papers presented on that occasion. (A paperback version, perhaps more modestly priced, constitutes a volume in Series A of the *Philosophical Transactions of the Royal Society*¹.)

The symposium marked the 20th anniversary of the invention of radiocarbon dating and the first seven papers, beginning with a useful and readable review article by Willard F. Libby, are devoted to this topic. Perhaps a little of the symposium's thunder was stolen by the twelfth Nobel

Symposium on "Radioactive Variations and Absolute Chronology", held at Uppsala only four months previously, when the scientific problems relating to ¹⁴C were discussed in greater technical detail. But the object of the London symposium was not the same, and this book is an attempt to bridge the gap which too often separates the archaeologist and his scientific colleagues. In general, because most of the contributors were at pains above all to be lucid, it succeeds admirably.

The chapters on dating include a beautifully concise survey of Egyptian calendrical chronology by I. E. S. Edwards, and the first publication by him and by Rainer Berger of the determinations made in the radiocarbon laboratories of the British Museum and the University of California at Los Angeles. The dates, from early contexts specially selected by Geoffrey Martin, tie in fairly well with the new tree ring calibration of radiocarbon. Sir Harry Godwin contributes a useful survey of the radiocarbon chronology of prehistoric Britain, and the picture is enlarged by chapters on thermoluminescent dating and on changes in the Earth's magnetic field intensity. All this gives the most convenient summary available of the present position in the field of scientific dating. At a time when the bristlecone pine calibration of radiocarbon dating is exciting so much interest, however, papers specifically on bristlecone pine dendrochronology and the resulting calibration would have been very welcome. Indeed, two of the people most suitable to give them, Bryant Bannister and Hans E. Suess, were apparently present at the meeting, the latter contributing a very brief but illuminating intervention published in this volume.

The truly heartening thought provoked by these papers, which include considerations of archaeological prospecting and of the various analytical techniques available for the examination of artefacts, is that archaeological technology today really has grown beyond the development stage. Indeed, second generation techniques are now replacing the exploratory demonstration of basic principles. Radiocarbon dates can be calibrated, fine grain and inclusion dating techniques in thermoluminescence replace the simpler holistic approach to pottery dating, and progress in archaeological surveying now comes primarily from improvements in the software of data processing techniques rather than from the hardware of the basic instrumentation.

Inescapably perhaps (or is it so inevitable?) the running seems to be made by the natural sciences—only four professional archaeologists contribute to the volume as against thirteen scientists, and two of these four write about methods and techniques of investigation rather than their results. The symposium was

thus really about methods for archaeology, not results in archaeology.

This does not, however, mean that the book is of interest only to the archaeologist. For the high calibre of the scientific contributors shows, above all, that archaeology really has taken its place in the scientific community as a recognized and valid subject of inquiry, a field for serious and sustained research and not merely a harmless and diverting hobby for research workers in their lighter moments. The dedicated professionalism of the work here, and the recognition accorded it by our two principal learned societies, promises well for the future.

The book lacks an index, and, more seriously, some of the contributors were evidently not asked to supplement their papers with bibliographical references. These defects apart, this volume is an altogether fitting monument to a historic occasion, and a gratifying demonstration of the high quality of scientific collaboration which archaeology can now attract.

COLIN RENFREW

¹ *Phil. Trans. Roy. Soc. A.*, **269**, 1 (1970).

Giants in Alliance

Imperial Chemical Industries: a History. Volume 1: The Forerunners 1870–1926. By W. J. Reader. Pp. xvi + 563 + 38 plates. (Oxford University: London, October 1970.) 120s.

Anatomy of a Merger: a History of GEC, AEI and English Electric. By Robert Jones and Oliver Marriott. Pp. 346 + 23 illustrations. (Cape: London, October 1970.) 75s.

MERGERS and amalgamations were a common feature of British industrial history in the inter-war years. Neither the causes nor the consequences, particularly the latter, have been thoroughly investigated to date, though one can easily speculate on the forces which prompted firms to merge their interests—sagging profits, excess capacity and increasing competition. When one turns to individual case histories such generalizations often fail to do justice to the complex influences at work, though in the case of both chemicals and electrical products one factor, namely foreign competitive strength, appears to have exerted considerable pressure in the 1920s and early 1930s. The formation of ICI in 1926 might be seen as the logical culmination of the steady concentration of control in the chemical field in the previous half century, but in fact it was probably the emergence of the great German chemical combine, IG Farbenindustrie, which sparked off the need to produce a united British front. McGowan of Nobel Industries was the chief instigator of the all British combine as the answer to the Germans, though at one point there was a strong likelihood of British links with the IG group.

In the first volume of the history of ICI, Mr Reader examines in careful detail the growth and development of the four constituent companies of the company—Brunner, Mond, Nobel Industries, the United Alkali Co., and British Dyestuffs Corporation. The first two were undoubtedly the strongest companies, and their development before 1914 had been based on the exploitation of inventions in alkali and explosives respectively. The success of Brunner, Mond in ammonia soda spelled the decline of the traditional Leblanc soda producers who in defence consolidated their interests in 1890–91 with the formation of the United Alkali Company which subsequently became the “ailing giant” of the chemical industry. British Dyestuffs Corporation, a more recent but none too viable creation, emerged as a response to Government initiative as a consequence of the serious lag in synthetic dyestuffs production in Britain and the termination of German supplies during the war.

The author has been given a free hand in the use and interpretation of the companies' records and this is clearly reflected in some of the more unsavoury disclosures, particularly the unethical attempts made by Brunner, Mond to get hold of the secrets of synthesizing ammonia from Germany after the war which virtually amounted to pillaging the vanquished, and the same company's long-drawn-out business battle with Lever Brothers which badly tarnished the image of Brunner, Mond.

Undoubtedly, Mr Reader's volume deserves to rank among the leading business histories; it is a story well told and it is to be hoped that the achievements of ICI will be exposed to rigorous analysis in a subsequent volume. Some reservations need to be made about the first volume, however. It is primarily a narrative account and only a limited effort is made to analyse the long-run performance of the companies before 1914 or to quantify the effects of the firms' policy decisions. A considerable amount of statistical data is relegated to the appendix with insufficient comment in the text. There is, moreover, scarcely any mention of the workers employed in the industry. On the other hand, Mr Reader devotes undue attention to the complex system of trading agreements while the overall background development of the chemical industry is inadequately explored, though this type of failing is common to many business histories. Finally, there are one or two misleading generalizations, the most notable being the notion that there was a smooth and self-regulating system of international exchange before 1914 (page 168 and repeated again on page 324).

Some of the characteristic features in the development of the chemical industry have their parallels in the electrical manufacturing industry. The latter industry became riddled with a network of

restrictive trading agreements and alliances which were international in scope; foreign competition and influence were strong—especially the American, which controlled a substantial slice of the industry before 1939, while this industry has also been characterized by successive waves of mergers and take-overs. The most spectacular have been the recent acquisition of AEI and English Electric by GEC under Arnold Weinstock. Jones and Marriott trace the background to these events through the histories of GEC, formed in the late nineteenth century by a German émigré, Hugo Hirst, English Electric, a merger effected in 1919 out of “a hotchpotch of companies . . . the roots of which reached back well into the nineteenth century”, and AEI, an amalgam of British Thomson-Houston and Metrovick in 1928. The battle for control of electrical companies in the 1920s does offer something of a contrast to that in chemicals. In the former case British interests were not able to present a united front to rebuff American control. In fact, so strong was the US influence that it was the General Electric Company of America under the ruthless leadership of Gerard Swope that engineered the merger of 1928. Indeed, Swope had much more ambitious plans which, though they did not materialize, were designed to achieve the very same grouping that Weinstock managed to accomplish in the late 1960s.

As the authors show, the fortunes of the companies varied a great deal up to the time of their fusion, and the intricate and complex share-dealings, take-overs, trading agreements and company alliances together with the personalities involved are described in lively detail. Though this provides an interesting, even entertaining, narrative, the book as a whole is not altogether satisfying. It does not provide much information about the general development of electrical manufacturing in this country and few statistical data relating to the companies concerned are provided. It is true that quite a lot of data on profits are scattered about the text but there are few long-run comparative series, and as it is not always clear what basis of measurement is being used, the figures are not very meaningful. Given the paucity of good histories on electrical manufacturing it is a pity that the authors did not see fit to provide rather more background information.

DEREK H. ALDCROFT

Muscle Spindles

The Basis of Motor Control: Integrating the Activity of Muscles, Alpha and Gamma Motoneurons and their Leading Control Systems. By Ragnar Granit. Pp. vii + 346. (Academic: London and New York, November 1970.) 100s; \$14.50.

As one reads this book one cannot help but compare it with *Receptors and*

Sensory Perception by the same author, written fifteen years previously. Although it was only in part concerned with muscle receptors, the enthusiastic way in which Granit wrote about them must have captured the interests of many research workers. It is tempting to speculate how much of the vast amount of new work on the subject owes its origin to some stimulus from that book. Much of the present book has a less relaxed style, and large parts of it are straight review with a too high ratio of references to text to make for easy reading. As Granit says in the preface, “The subject is virtually boundless”. How then does he select his material? Quite simply he restricts himself to those topics which have interested him, and makes no pretence at being comprehensive; much of the book is thus constructed around a framework of papers from the Neurophysiological Nobel Institute. The approach is that of classical physiology and the thesis is the importance of muscle spindles.

The first six chapters deal with muscles, muscle spindles and tendon organs, the properties of muscle spindles with and without fusimotor innervation, the organization of motoneurone discharges and the effects of muscle receptor impulses upon these discharges. Chapter seven discusses the control of posture and movement by muscle spindles in the more relaxed way found in *Receptors and Sensory Perception*. This contains Granit's own notions, and is the one I should recommend a student to read first. Having seen the wood he would then be motivated to do the hard work on the trees in the preceding chapters. Incidentally Granit says in his preface that “this book requires some basic knowledge of physiology”. With his excellent knowledge of English, Granit has also acquired the capacity for understatement. The book is a valuable one for teachers and postgraduates but undergraduates will require very careful guidance.

There is a whole chapter devoted to the control of intercostal muscles and the diaphragm, and one to eye movements and stepping. The main theme of the importance of muscle spindles predominates throughout. The fact that the central nervous system above the neck is dealt with in less than fifty pages perhaps reflects the tendency of workers in these difficult fields to ignore the importance of muscle spindles and their motor innervation. Granit has never committed himself wholeheartedly to the servo theory for the control of muscle shortening. In his final chapter Granit refers to the “servo hypothesis” and proceeds to discuss it in very general qualitative terms. One gets the impression that the author is not very happy in this branch of engineering, and prefers the familiar waters of classical physiology. Occasion-

ally there are examples of special pleading. Granit complains of neglect to read carefully the papers containing evidence in favour of alpha innervation of intrafusal muscle fibres. Certainly the experiments of Barker and Laporte and their respective co-workers leave no doubts in our minds that some motor fibres, larger than gamma, branch to supply both intra and extrafusal muscle. The more carefully one reads these papers, however, the more one doubts whether the early response of the primary spindle afferent fibres is due to an alpha motor innervation. Only more direct evidence on this point will convince the sceptics and perhaps it is with the hope of promoting fresh experiment that Granit writes so challengingly. Indeed, throughout the book ideas for future experiments are tossed about. The general has retired but he leaves no doubt where his successors should attack.

The book is on the whole well produced, the bibliography is extensive and well indexed. This alone will make it invaluable in teaching. Some illustrations are substandard. A full page reproduction of a figure from Boyd's work in the *Philosophical Transactions of the Royal Society* is rendered meaningless, the more the pity, for the journal is not available in all libraries. Some illustrations lose their impact by excessive reduction, and one cannot help feeling that legends which are suitable in the original paper are not always so in a work such as this. Having pointed out some blemishes I rush to say that I would unhesitatingly recommend the book to neurophysiologists, to neurologists with a good grounding in neurophysiology and possibly to engineers—but they may need a guiding hand. J. E. PASCOE

Population Control

The Growth and Control of World Population. By W. D. Borrie. (The Advancement of Science.) Pp. x+340. (Weidenfeld and Nicolson: London, November 1970.) 60s.

Books on "the population problem" seem to be growing at a rate similar to their subject matter. Demography is no longer the Cinderella of the social sciences, and though it would be immodest to agree with the jacket of this book that it is "the important subject", it is flattering that it should be so described. Inevitably, with the growth of public interest, it is the extremist prognoses which receive the greatest attention. At present it is the prophets of unmitigated doom who hold the stage, but there are also those eternal optimists who believe that the problem will solve itself. There is a great need for a concise introduction to the current demographic situation of the world which, while giving consideration to the views of the extremists, does

not lie in either camp. This book fulfils that need.

Professor Borrie sets out to examine the chief demographic themes in history which have led to the current situation; this is mapped out in chapters devoted to the demographic patterns of the three third world continents, Europe and overseas European countries. A point which is well brought out in this book, but which is often overlooked, is the particular demographic features of each of the third world continents—features which are as important as the general similarities. Africa still has unacceptably high mortality rates and the potential for growth there has not yet been fully realized. South America may be able to accommodate its natural increase for a short time, though a limitation which Borrie does not discuss is the rapid rate of urbanization and the demographic consequences of this process. In fact, greater attention could have been paid to the general subject of urbanization and the distribution of population concentrations within countries, while the length of the chapter on the great overseas migrations, which are essentially of the past, could have been reduced. This disproportionate attention to European overseas migration is understandable, however, as the author comes from the Australian National University.

Although the current emphasis in demographic work is on the need for fertility reduction, Borrie shows that throughout the third world, levels of life expectancy are still unacceptably low. Increases in life expectancy must to a degree increase the difficulty of fertility reduction, for third world countries are still a long way from the state of "demographic immortality", a somewhat obscure term he uses to mean the situation where virtually every person born can expect to survive to the end of their reproductive period.

The chapter on "Population Policies and the State" shows how specific governmental policies have had little effect on the change from high to low and controlled fertility, although measures primarily adopted for socio-medical reasons, such as legalizing abortion, have sometimes had demographic side effects. Measures to reduce further fertility levels in western countries would have to go beyond the generally accepted limits of democratic government.

The introduction of the demographic concept of life expectancy, and its symbol (e_0^0), without explanation early in the book should have been avoided. A misreading of a full stop as a zero has inflated Ceylon's population on page 118 to 607 million (standing room only, indeed), while the first truly national census in 1703 was in Iceland and not Ireland as stated on page 23. These are, however, small points which cannot detract from a refreshing book which

concludes by pointing out that the demographic growth rates of today are a reflexion of the triumph of man over environment, through the application of science. The triumph still has to be completed by bringing fertility into line with low mortality levels and, to achieve this, third world countries must follow a course not taken by the west; the reduction of fertility before the general spread of the social and economic consequences of industrial growth, but premonitions of failure are as yet unjustified.

D. R. COPE

Theory of Coherence

Coherent Light. By A. F. Harvey. Pp. xxxvi+1329. (Wiley Interscience: London and New York, December 1970.) 360s.

It is in no way disparaging to say that the most valuable thing about this book is its list of references. On average something like 400 references are given at the end of each of the twenty-eight chapters. As the reference includes not just the author and journal but also the title of the paper cited, the value of such a bibliography, based as it is primarily on work of the last ten years, cannot be over estimated.

Dr Harvey has produced an enormous volume of a size which is usually produced by a group of authors coordinated by an editor. The fact that he has compiled the volume single-handed would lead one to hope that the overall content should be more of a piece than one usually expects in a wide-ranging volume of this kind, and the hope is justified. The title of the book, however, is somewhat misleading. The theory of coherence from a classical standpoint is certainly much better reviewed in chapter 10 of Born and Wolf's *Principles of Optics*, and the quantized field approach of Glauber is simply not reviewed in this book at all.

The title in fact seems not to explain very well the author's intentions. He sets out to compile a detailed account of the work associated with the creation and use of sources possessing spatial and temporal coherence in the range from submillimetre waves to the ultraviolet, and chooses to aim at the engineer or applied physicist using the devices rather than the physicist concerned with fundamental ideas. Consequently the theory of coherence, of lasers and of non-linear optics are all better expounded in other books. But at the level chosen, and given the splendid bibliography, the volume is undoubtedly a valuable source of reference. The author is well served by his publisher in terms of the quality of the production, but at this price presumably even some libraries will ask themselves if they are not better off buying three or four other books in this area for the same money.

L. ALLEN

CORRESPONDENCE

Johannesburg Observatory

SIR,—It may surprise you to learn that your editorial "Good Cheer for Astronomers" (*Nature*, 228, 316; 1970) has been read with very mixed feelings not only in South Africa but also abroad. Indeed, one foreign astronomer felt strongly enough to airmail us, on his own initiative, an advance copy on which he had deleted the word "Good" and substituted "Bad".

On the face of it there should be nothing but praise for the agreement between the Science Research Council and the South African Council for Scientific and Industrial Research "to merge the facilities at the Royal Observatory at the Cape and at the Republic Observatory in Johannesburg into a single station situated near Sutherland some 250 miles north-west of Cape Town" (*Nature*, 228, 5; 1970). Certainly, nobody would criticize the decision to embark on a policy of vigorous development of astronomy in South Africa, and nobody would begrudge the Cape Observatory a new lease of life if that should be one result of the decision. However, there are several less happy aspects of the agreement that have given rise to considerable adverse criticism, and even resentment, in local circles.

Among the criticisms that have been voiced are the failure of the CSIR (who have no astronomers in their executive) to consult representative astronomical opinion in this country, and the choice of Sutherland as the site of the outstation, however convenient it may be for the immediate needs of the Cape Observatory.

But the main criticism is the decision to close the Republic Observatory, founded in 1903 and the national observatory for 60 years. It was a government institution until 1964 when it was transferred to the CSIR. As a national observatory it has hitherto concerned itself mostly (but by no means wholly) with the long-term astrometric programmes characteristic of such institutions—if they do not shoulder the burden, who will? Its main activities have been in the fields of visual double stars (observational and theoretical) and minor planets and comets. We do not think that we shall be accused of vain boasting

if we say that in these activities the Republic Observatory with two or three other observatories has led the world and can well continue to do so.

It is somewhat misleading to say that "the Republic Observatory in Johannesburg has also fallen a victim to city light". The 26.5 inch refractor, with which the observatory built up its reputation in double-star observation, is little, if at all, affected by sky illumination or smog and the time-tested "seeing" remains as good as ever. There is no reason why it should not be usefully employed in this work, at its present site, for many years to come. There is as little reason to move it to a new and relatively untested site as there would be in the case of the refractors similarly employed at Meudon (only 7 km from the Eiffel Tower), Nice, or Washington, DC. For those programmes that really are affected by deterioration of the night-sky the observatory has an annexe in pleasant surroundings at Hartbeespoort, a mere 50 miles from Johannesburg. Here the sky is adequately dark for all but the most exacting astrophysical requirements, as evidenced by the sophisticated photoelectric photometry carried out by the Leiden Observatory Southern Station on the same site.

Yet the Republic Observatory is to be broken up as a corollary, apparently regarded as axiomatic, of the SRC-CSIR agreement (there is no question of comingling between Johannesburg and Sutherland as suggested in your editorial, for the intention is definitely to close the observatory). We are told that one (or two?) telescopes and, we imagine, some smaller items will be salvaged for the new observatory, and such members of the staff as have not resigned will be transferred to Cape Town. The rest of the equipment together with the accumulated experience and tradition will be dispersed. The Witwatersrand, the most densely populated area of the republic, with five universities in its environs, will lose an important civic and educational amenity. To break up an active institution whose days are certainly not numbered for the little that the new institution can salvage from it seems both senseless and wasteful.

Even if the observatory were moved *en bloc* to Sutherland it would remain more than doubtful, whether its largely

astrometric programmes could be continued there as successfully as in Johannesburg and Hartbeespoort. The "seeing" is known to be good in Johannesburg but we have little evidence that this is the case at Sutherland. The minor planet work would be seriously affected by transfer from the clear winter skies of the high veld, of that there is no doubt, for it is in winter when the ecliptic is south of the equator at night that the programme reaches its peak. Furthermore, double-star work in particular is of an intensive, long-term and personal nature, and the parties to the agreement themselves admit that Sutherland is not a suitable site for permanent residence of the observers and their families. In fact, the decision to concentrate South Africa's contribution to astronomy to any one site, whether at Sutherland or elsewhere, flouts a principle that is being increasingly stressed: that it is wholly unrealistic to look for a "polyvalent" site ideal for every kind of astronomical activity.

The CSIR seem to be very reluctant to reconsider their decision to close the Republic Observatory, perhaps because they feel that this would be a repudiation, in some degree, of their agreement with the SRC. It would therefore be a gracious gesture, and one that would earn much goodwill in this country, if the SRC took the initiative and indicated their unwillingness to profit from the "cannibalizing" of an observatory that is perfectly viable and by no means ready for the scrap heap.

Yours faithfully,

W. H. VAN DEN BOS

Director, Republic Observatory, 1941–56,
"Ons Tuis,"

1 Observatory Avenue,
Observatory,
Johannesburg

W. S. FINSSEN

Director, Republic Observatory, 1957–65,
PO Box 4204,
Johannesburg

TH. WALRAVEN

Astronomer in charge,
Leiden Observatory,
Southern Station,
PO Box 13,
Broederstroom,
Transvaal

Obituary

Dr C. N. H. Long

HUGH LONG, the endocrinologist, and Sterling Professor Emeritus at Yale, died suddenly at Pennaquid Beach, Maine, on July 6, 1970, at the age of sixty-nine.

Born in Nettleton, England, he began his education in science at Manchester University in organic chemistry. After receiving his MSc in 1923, Long went with A. V. Hill to the Department of Physiology, University College, London, where he took part, with Hill and Lupton, in the work on the biochemistry of muscular exercise and fatigue in man, supported by the Industrial Fatigue Research Board.

In 1924 he was elected a member of the Physiological Society. That year, on appointment as lecturer in medical research, Long entered the Medical School at McGill and after receiving his MD in 1928 stayed on as a member of the Department of Medicine. With J. Beattie and G. R. Brow he studied the action of anaesthetics on skeletal muscle and on the heart, with results which led to the report that chloroform induces extra systoles by an action via the hypothalamus. These studies by Beattie, Brow and Long are among the last of the significant papers on hypothalamic physiology before the "stereotaxic era"

was opened by S. W. Ranson and his associates.

In 1932 Dr Long was appointed director of the Cox Institute of Medical Research, a small endowed laboratory attached to the Department of Medicine at the University of Pennsylvania. Housay and Biassotti had just discovered that hypophysectomy ameliorates the metabolic effects of pancreatectomy in toads and dogs. Two years later Long, with Lukens, an instructor in the Department of Medicine, reported that adrenalectomy also "alleviates" the diabetes of depancreatized cats, and suggested that this effect is brought about by the decreased production of glucose and ketone bodies rather than by restoration of glucose utilization. By selective operations they were able to attribute the alleviation of the diabetic condition to removal of adrenal cortex rather than medulla.

After his appointment in 1936 to the faculty of Yale University School of Medicine, on which he served until he retired in 1969, first as professor and chairman of the Department of Physiological Chemistry (1936-51), then as dean (1947-51) and later as professor of physiology (1951-69) and chairman of the department (1951-64), Long continued to focus his research interests on the adrenal gland. During the Second

World War, when he became a citizen of the United States, Long directed research in his department on the endocrine status and intermediary metabolism of animals subjected to haemorrhage, in the course of which a study was made of the action of ACTH in depletion of the cholesterol content of the adrenal cortex and later the depletion of ascorbic acid; this led to a standard test for adrenal cortical activation. Long was also interested in the possibility of a neural component in the activating system, and hypothesized that epinephrine might be the common denominator of the great variety of conditions known to stimulate the hypophysial-adrenal system. His last research, in collaboration with Ora Kingsley Smith, dealt with the endocrine status of the "visceral organism", a preparation developed under his direction by T. Hiroshige for perfusing the abdominal and thoracic viscera under conditions in which their metabolic interaction could be analysed.

Honorary degrees were conferred on Dr Long by Princeton, McGill and the University of Venezuela. He received the Banting Memorial Medal of the American Diabetes Association in 1951 and was a member of the National Academy of Sciences, the American Academy of Arts and Sciences and the Philosophical Society.

Announcements

University News

Dr H. D. Suit, University of Texas, has been appointed professor of radiation therapy and chief of the Department of Radiation Medicine at the Massachusetts General Hospital, **Harvard University**.

Dr Rainer Goldsmith has been appointed to the chair of physiology at Chelsea College of Science and Technology, **University of London**, and **Dr J. A. S. Smith** has been appointed to the chair of chemistry tenable at **Queen Elizabeth College**.

Appointments

Nathan M. Pusey, president of Harvard University, will succeed **Charles S. Hamilton** as president of the **Andrew W. Mellon Foundation**.

Professor G. A. Barnard, University of Essex, **Mr D. J. Barron**, York University, and **Professor W. G. McClelland**, Man-

chester Business School, have been appointed members of the **Social Science Research Council**.

Dr Melvin N. A. Peterson has been appointed co-principal investigator of the Deep Sea Drilling Project, which is managed by the **Scripps Institution of Oceanography** under contract to the US National Science Foundation. **Dr N. Terence Edgar** will succeed **Dr Peterson** as chief scientist of the project.

Miscellaneous

The **CIBA medal and prize** for 1970 has been awarded by the Biochemical Society to **Professor D. C. Phillips**, University of Oxford. The **Colworth medal** of the Society has been awarded to **Dr D. A. Rees**, Unilever Research Laboratory, and the **Gowland Hopkins medal** to **Dr F. Sanger**, MRC Laboratory of Molecular Biology.

The British Nutrition Foundation will present an award of £1,000 annually for the next five years to individual scientists for distinguished research in nutrition. The first recipient of the award, to be

known as the British Nutrition Foundation prize, is **Professor R. A. McCance**, University of Cambridge.

ERRATUM. In the article "Kinetic Mass Spectrometric Study of the Flash Photolysis of NO₂" by J. N. Bradley, W. D. Capey and J. R. Gilbert (*Nature*, **229**, 41; 1971), the following corrections should be made. The sentence beginning on line 10 of the first paragraph should read "The sampling nipple . . ."; line 13 of paragraph 5 should read ". . . and this seems most unlikely 100 ms after flash"; the end of the penultimate sentence should read ". . . produces NO₂ in the presence of NO (ref. 8)".

ERRATUM. In the article "Trials with a Transponding Acoustic Fish Tag tracked with an Electronic Sector Scanning Sonar" by M. Greer Walker, R. B. Mitson and T. Storeton West (*Nature*, **229**, 196; 1971), the last figure in the last column of Table 1 should be 1.46.

British Diary

Monday, February 1

Chatting to Computers (6.30 p.m.) Dr C. R. Evans, Institution of Electrical Engineers, London Graduate and Student Section, at Savoy Place, London WC2.

Difficulties Inherent in the Study of Gas Exchange and Circulation of Blood in the Lungs (6 p.m.) Dr H. N. Duke, University of London, at the Royal Postgraduate Medical School, Du Cane Road, London W12.

Modern Electric Motor Protection (7 p.m.) Mr W. J. Johnson, Institution of Electrical Engineers, at the Royal Star Hotel, Maidstone, Kent.

Pre-Service Component Testing of Steam Power and Process (6.15 p.m.) Mr A. J. Morton, Institution of Mechanical Engineers, at the University of Durham.

Some Aspects of the Chemistry of Metal-Olefin Complexes (6.30 p.m.) Professor Sir Ronald Nyholm, FRS, Society of Chemical Industry, at the Scientific Societies Lecture Theatre, 23 Savile Row, London W1 (Jubilee Memorial Lecture).

The Use of Instrumentation in the Evaluation of Paint Performance (7 p.m.) Mr D. M. Bishop, Oil and Colour Chemists' Association, at the Bullock Lecture Theatre, Hull College of Technology.

Tuesday, February 2

Abstraction in Science and Morals (5 p.m.) Dr K. Korner, in Room 9, Mill Lane Lecture Rooms, Cambridge (Twenty-fourth Eddington Memorial Lecture).

Decimalization—the Nineteenth-Century Debates (1.20 p.m.) Dr W. A. Smeaton, University of London, in the Botany Theatre, University College London, Gower Street, London WC1.

Some Aspects of Adrenal Pathology (5.30 p.m.) Dr T. Symington, University of London, at the Institute of Child Health, 30 Guilford Street, London WC1 (Eighth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation).

The Neolithic Encampment on Lake Fimon, Northern Italy (5.45 p.m.) Mr L. H. Barfield, University of London, at the Institute of Archaeology, 31–34 Gordon Square, London WC1.

The Psychology of Prejudice with reference to Race Relations in the United Kingdom (5.15 p.m.) Dr D. I. Brough, Royal Society of Arts, John Adam Street, London WC2.

What is the Current Barrier to Higher Engines Ratings and how Important is it to Break It? (6 p.m. discussion) Institution of Mechanical Engineers, at 1 Birdcage Walk, London SW1.

Wednesday, February 3

Bone in Organ Culture (11 a.m.) Dr J. J. Reynolds, University of London, at the Institute of Orthopaedics, 234 Great Portland Street, London W1.

Colour in Therapy (3 p.m.) Mr M. H. Wilson, Colour Group (Great Britain) in the Physics Department, Imperial College, Prince Consort Road, London SW7.

Electronic Scanning Systems (6 p.m.) Mr M. F. Radford, Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

John Greaves (1601–1652) and the Translation of Islamic Astronomical Works (1 p.m.) Mr Francis Maddison, Royal Institution, History of Science Discussion Group, at 21 Albemarle Street, London W1.

Live Line and Bare-Hand Working on High Voltage Systems (7.30 p.m.) Mr J. S. T. Looms and Mr A. R. Barber, Institution of Electrical Engineers, at the CEGB, Guildford, Surrey.

Motivation in the Seventies (all-day discussion) Institution of Mechanical Engineers, at 1 Birdcage Walk, London SW1.

Surface Coatings to Combat Wear (6 p.m. discussion) Institution of Mechanical Engineers, at 1 Birdcage Walk, London SW1.

The Determination of Small Amounts of Anions (6.30 p.m.) Mr G. Svehla, Mr R. M. Dagnall and Mr W. I. Stephen, Society for Analytical Chemistry, at the Scientific Societies Lecture Theatre, 23 Savile Row, London W1.

The Thames Barrier Investigation (7.15 p.m.) Mrs M. Kendrick, Women's Engineering Society, at "Hope House", 45 Great Portland Street, London SW1.

Thursday, February 4

Art and Science: 4. Art in the Age of Reason—The Mechanical World of Descartes and Newton (1.30 p.m.) Mr P. D. Carpenter, University of London, at Imperial College, London SW7.

Biosynthesis and Adrenocorticosteroids (5.30 p.m.) Dr J. K. Grant, University of London, at the Institute of Child Health, 30 Guilford Street, London WC1. (Ninth of fifteen lectures on "The Scientific Basis of Medicine" organized by the British Postgraduate Medical Federation.)

Can Large Mammals Survive in the Wild? (1.20 p.m.) Dr P. A. Jewell, University of London, in the Botany Theatre, University College London, Gower Street, London WC1.

Design Implications of In-Service Inspection (6 p.m. discussion) Institution of Mechanical Engineers, at 1 Birdcage Walk, London SW1.

Flooring Compositions (6.30 p.m.) Oil and Colour Chemists' Association, at the Royal Turks Head Hotel, Grey Street, Newcastle upon Tyne.

Properties of Matter. Part 1: Solids, Liquids and Gases. Part 2: Atoms and Molecules (1 p.m. films) Royal Institution, at 21 Albemarle Street, London W1.

The Refiner's Fire: the Enigma of Alchemy in East and West (6 p.m.) Dr Joseph Needham, University of London, at Beveridge Hall, Senate House, London WC1.

The Problems of Managements in a Modern Setting (5.30 p.m.) Mr A. R. Cooper, Institution of Electrical Engineers, at Savoy Place, London WC2.

Friday, February 5

Some Facts of Life—Biology and Politics (9 p.m.) Sir Hans Krebs, FRS, Royal Institution, at 21 Albemarle Street, London W1.

Uses of Photoenolisation in Organic Syntheses (1 p.m.) Dr P. G. Sammes, Royal Institution, Photochemistry Discussion Group, at 21 Albemarle Street, London W1.

Saturday, February 6

The Hong Kong New Territories and Their People (3.30 p.m.) Professor Maurice Freedman, Inner London Education Authority, at the Horniman Museum, London Road, Forest Hill, London SE23.

Monday, February 8

Absorption of Hydrocarbons on to Oxide Surfaces Related to Road Building Materials (5.50 p.m.) Mr D. M. Colwill and Dr P. C. Thompson, Society of Chemical Industry, at 14 Belgrave Square, London SW1.

Effects of Rotor Eccentricity on Acoustic Noise from Induction Machines; and Natural Frequencies of Stators of Small Electric Machines (5.30 p.m.) Dr A. J. Ellison and Dr S. J. Yang, Institution of Electrical Engineers, at Savoy Place, London WC2.

On the Nature of Linguistic Evidence (5.30 p.m.) Dr P. Seuren, British Society for the Philosophy of Science, in the Joint Staff Common Room, University College London, Gower Street, London WC1.

Stored Program Control Application in Telephone Switching (5.30 p.m.) Mr N. Ward, Institution of Electrical Engineers, Savoy Place, London WC2.

Reports and Publications

not included in the monthly Books Supplement

Great Britain and Ireland

History of Science and Technology: a Select Bibliography for Students. By K. J. Rider. Second edition. Pp. 75. (London: The Library Association, 1970.) 15s (12s LA members). [1412]

Department of Education and Science, Architects and Building Branch. Design Note No. 6: Sedgefield School, Durham. Pp. 44. (London: Architects and Building Branch, Department of Education and Science, 1970.) *gratis* [1412]

Nucleic Acids Abstracts, Vol. 1, No. 1, January 1971. Published monthly. Pp. 1-74. Subscription rates: Europe £30; Outside Europe US \$150 (airmail/airfreight delivery). (London: Information Retrieval Limited, 1970.) [1512]

Of Mice and Men. By Professor D. G. Harnden. (An Inaugural Lecture delivered in the University of Birmingham on 7th May 1970.) Pp. 15. 4s; \$0.48. (Chemically Reactive Polymers. By Professor Sydney Alan Barker. (An Inaugural Lecture delivered in the University of Birmingham on 19th May 1970.) Pp. 14. 4s; \$0.48. Why Mathematics? By Professor Brian Kuttner. (An Inaugural Lecture delivered in the University of Birmingham on 21st May 1970.) Pp. 11. 4s; \$0.48. (Birmingham: The University, 1970.) [1512]

Regional Policy in Britain and the Six: The Problems of Development Areas. By Harold Lind. Community Regional Policy. By Christopher Flockton. (European Series, No. 15.) Pp. 76. (London: Chatham House and PEP, 1970.) 13s [1512]

Central Statistical Office. Social Trends, No. 1, 1970. Edited by Muriel Nussel. (A publication of the Government Statistical Service.) Pp. 181. (London: HMSO, 1970.) 65s net. [1512]

Building Research Station. Current Paper 35/70: Wind Loading on Vickers Tower, Millbank. By C. W. Newberry, K. J. Eaton and J. R. Mayne. Pp. 8. (Reprinted from *Building*, Vol. 219, No. 6639, 14 August 1970.) (Garston, Watford: Building Research Station, 1970.) *gratis* [1612]

Department of Education and Science. Teachers Course List No. 1: Programme of One Year Courses and One Term Courses for Qualified Teachers, 1961-72. Pp. 104. Teachers Course List No. 2: Programme of Short Courses, April 1971-March 1972, organized by the Department for teachers and others engaged in the educational service in England and Wales. Pp. 59. (London: Department of Education and Science, 39 York Road, SE1, 1970.) *gratis*. [1612]

Third Report of the Countryside Commission for the year ended 30 September 1970. Pp. vi+76+13 photographs. (London: HMSO, 1970.) 13s (65p) net [1712]

Report of The Committee of Enquiry into the Relationship between University Courses in Chemistry and the Needs of Industry. Pp. vii+337. (London: Royal Institute of Chemistry, 1970.) 40s [1712]

Philosophical Transactions of the Royal Society of London: A: Mathematical and Physical Sciences. Vol. 269, No. 1193, (17 December 1970): A Symposium on the Impact of the Natural Sciences on Archaeology. Organized jointly for the Royal Society and the British Academy by T. E. Allibone, FRS, Sir Mortimer Wheeler, FRS, I. E. Edwards, E. T. Hall and A. E. A. Werner. Pp. 1-185+plates 1-3. (London: The Royal Society, 1970.) 100s; \$13. [1712]

Glasshouse Crops Research Institute. Annual Report 1969. Pp. 182. (Rustington, Littlehampton: Glasshouse Crops Research Institute, 1970.) 20s. [1812]

The University of Hull. Annual Report 1969/70. Pp. 163. (Hull: The University, 1970.) [1812]

UKAEA: Research Group. AERE-R 6556: Radioactive Fallout in Air and Rain—Results to the middle of 1970. By R. S. Cambray, Miss E. M. R. Fisher, W. L. Brooks and D. H. Peirson. Pp. iii+46. (Harwell, Berks: Health Physics and Medical Division, AERE, 1970. Available from HMSO.) 8s net. [1812]

Other Countries

US Department of the Interior: Geological Survey. Water-Supply Paper 1999-E: Mean Annual Runoff as Related to Channel

Geometry of Selected Streams in California. By E. R. Hedman. Pp. iii+17. \$0.25. Professional Paper 433-K: Stream Dispersion at Selected Sites. By Richard G. Godfrey and Bernard J. Frederick. Pp. iv+38. \$0.55. Professional Paper 529-G: Atlantic Continental Shelf and Slope of the United States—Heavy Minerals of the Continental Margin from Southern Nova Scotia to Northern New Jersey. By David A. Ross. Pp. iv+40. \$0.50. Professional Paper 635: Uppermost Cretaceous and Tertiary Stratigraphy of Fossil Basin, Southwestern Wyoming. By Steven S. Oriel and Joshua I. Tracey, Jr. Pp. vi+53. \$0.65. Professional Paper 700-C: Geological Survey Research 1970, Chapter C—Scientific Notes and Summaries of Investigations in Geology, Hydrology, and Related Fields. Pp. v+251. \$3.25. (Washington, DC: Government Printing Office, 1970.) [912]

Illinois State Geological Survey. Environmental Geology Notes. No. 36: Geology for Planning at Crescent City, Illinois. Compiled by Robert E. Bergstrom. Pp. 15. No. 37: Distribution of Arsenic in Unconsolidated Sediments from Southern Lake Michigan. By R. R. Ruch, E. Joyce Kennedy and Neil F. Shimp. Pp. 16. No. 38: Petrographic and Mineralogical Characteristics of Carbonate Rocks Related to Sorption of Sulfur Oxides in Flue Gases. By Richard D. Harvey. Pp. 31. (Urbana, Ill.: Illinois State Geological Survey, 1970.) [1012]

Publications from the Cairo University Herbarium. No. 1: Street Trees in Egypt. By Dr. M. Nabil El-Hadidi and Dr. Loufy Boulos. Pp. viii+52 plates. No. 2: Alfred Kaiser's Sinai-Herbarium. By Vivi Tackholm. Pp. 181. (Giza: Herbarium, Botany Department, Faculty of Science, Cairo University, 1969 and 1970.) [1012]

Republic of South Africa: Department of Industries. Division of Sea Fisheries Investigational Report No. 85: Stock Assessment of the Pilchard *Sardinops ocellata* at Walvis Bay, South West Africa. By G. G. Newman. Pp. 13. (Sea Point, Cape Town: Division of Sea Fisheries, 1970.) [1112]

Australian Atomic Energy Commission. Eighteenth Annual Report 1969/1970. Pp. 128. (Coogee, NSW: Australian Atomic Energy Commission, 1970.) [1412]

HOW TO BUY NATURE

Volumes start in January, March, May, July, September and November. but subscriptions may begin at any time.

The direct postal price per subscription is:

12 MONTHS* (52 issues per title)

	Surface Mail UK and worldwide	Airfreight U.S.A Canada
Nature (Friday)	£14	\$48 \$52
Nature+		
Nature Physical Science	£24	\$83 \$90
Nature+		
Nature New Biology	£24	\$83 \$90
All three editions	£29 10s	\$108 \$116
Annual Index	£1	\$3 \$3

* Rates for shorter periods *pro rata* (minimum three months)
(Charge for delivery by air mail on application)

Editorial and Publishing Offices of "NATURE"

MACMILLAN JOURNALS LIMITED
4 LITTLE ESSEX STREET, LONDON WC2R 3LF
Telephone Number: 01-836 6633. Telegrams: Phusis London WC2R 3LF

Subscription Department

MACMILLAN JOURNALS LIMITED
BRUNEL ROAD, BASINGSTOKE, HANTS
Telephone Number: Basingstoke 5431

Advertisements only should be addressed to

T. G. SCOTT & SON, LIMITED
1 CLEMENT'S INN LONDON WC2A 2ED
Telephone 01-242 6264/01-405 4743
Telegrams: Textualist London WC2A 2ED

Registered as a newspaper at the Post Office

Copyright © Macmillan Journals Limited, January 29, 1971